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Bone and Joint Tuberculosis.—Two hundred cases of bone and joint tuberculosis in which the disease was proved at surgical operation or by postmortem examination have been studied. Of these cases, 100 were in children up to the age of sixteen and 100 were in adults. In the former group 70 per cent of the cases were in children under ten years of age. Among the adults 77 per cent of the cases were between the ages of sixteen and forty-five. The vertebral column was involved in 57 of the children and in 52 of the adults. Among other sites of involvement, the weight-bearing bones were more frequently found to be tuberculous in the adults than were the non-weight-bearing bones. Among the children there was a higher incidence of disease in the small tubular bones. Thirty-five per cent of the children and 28 per cent of the adults showed involvement of more than one bone or joint. In 42 per cent of the children and 55 per cent of the adults some form of pulmonary tuberculosis was discovered. Pleural effusions, genito-urinary tuberculosis, tuberculous peritonitis, meningitis and amyloidosis were complications that were frequently found. Paravertebral abscesses occurred in 28 of the 57 children with vertebral tuberculosis and in 37 of the 52 similarly affected adults. Involvement of the vertebral body may be in the anterior, central or posterior portions. Marginal involvement of the body occurs most frequently in adults and is usually associated with narrowing of the intervertebral disc. The central type of lesion is found chiefly in children. The diagnosis of tuberculosis of the bones or joints by the study of roentgenograms is very difficult since many other lesions cause similar appearing changes in the bones.—*A Statistical and Roentgenological Analysis of Two Hundred Cases of Bone and Joint Tuberculosis, L. Nathanson & W. Cohen, Quart. Bull. Sea View Hosp., January, 1941, 6: 148.*—(*A. A. E.*)

Tuberculosis of Bones.—Among 1,143 consecutive autopsies for tuberculosis there were 119 cases of skeletal tuberculosis, or 10.4 per cent. The youngest individual in this group was two years of age, the oldest sixty-seven. Fifty-nine of the cases, 49.6 per cent, were between twenty and thirty-nine years of age. Of the 119 cases, 22 had healed primary pulmonary foci; 13 cases showed evidence of chronic haematogenous tuberculosis; 33 had healed haematogenous foci; 15 had acute generalized miliary tuberculosis and 36 had chronic pulmonary tuberculosis. Tuberculosis of the urogenital system was found in 49 of the 119 cases. Tuberculosis of the bones in most cases originated in and often remained limited to the epiphyses. Diaphyseal involvement occurred most often in children and most frequently in the small bones of the hands and

feet. In 87 cases tuberculosis of the vertebrae was found, and in 19 tuberculosis of the ribs. Involvement of other bones was of much less frequent occurrence. Tuberculous infection of the bones may occur as a primary infection through the mucous membrane of the respiratory or digestive tracts, by lymphatic extension or by haematogenous infection. The latter route is by far the most frequent. In tuberculosis of the spine involvement is usually of more than one vertebra. The dorsal vertebrae are most frequently involved. The infection develops first in the vertebral body and involvement of the intervertebral disc occurs by direct extension. In the early stages the tuberculous process may be of a productive nature, although usually an exudative and destructive form of tuberculosis is encountered. The productive form of tuberculosis of the spine cannot be readily identified on roentgenograms since the infectious process is limited to the marrow spaces of the vertebral bodies and does not involve the intervertebral disc. Therefore the body of the vertebra and its adjoining cartilaginous disc are not altered in form. Roentgenological studies were made in 51 of the 87 cases of tuberculosis of the spine and a positive diagnosis of tuberculosis was made in 45 cases. In 6 cases tuberculosis of the spinous processes or transverse processes was found. Of the 87 cases with tuberculosis of the vertebral column, 83 had soft tissue abscesses in the region of the involved vertebrae. In most cases the abscess was bilateral and the course of the infection was first perforation of the anterior longitudinal ligament, followed by dissection of the pus in the connective tissue layers between the spinal muscles and in the fascial bands accompanying the large vessels and nerve trunks anterior to the spine. Rupture of such an abscess into the oesophagus was found in 2 cases. In 6 cases the abscess perforated into the lung. In the 19 cases with tuberculosis of the ribs there was tuberculous involvement of the vertebral column in 11. Amyloid disease was found in 42 of the 119 cases, or 35 per cent. The amyloid deposits were found chiefly in the liver, spleen, kidneys and adrenals. In 13.4 per cent of the 119 cases meningitis was the cause of death.—*Tuberculosis of the Skeletal System, O. Auerbach, Quart. Bull. Sea View Hosp., January, 1941, 6:117.*—(*A. A. E.*)

Cystic Tuberculosis of Bones.—For the past four years the writer had the opportunity of closely following the healing process, through roentgenograms, of widely disseminated cystic bone lesions of tuberculous origin in a six year old girl. The present concept of multiple cystic bone tuberculosis is applied to a comparatively rare form of diaphyseal bone tuberculosis, usually multiple, and of metastatic origin from a thoracic focus. Two main roentgen types are described; the diffuse and the circumscribed. The diffuse is the more acute initial stage, wherein the diaphysis cannot be differentiated into medulla and cortex and the cystic areas of decreased density are honeycombed with a web-like structure of increased density. The individual or several apertures in the web vary in size from that of a millet seed to that of a pea. The cystic areas may enlarge to include both medulla and cortex, increase the diameter of the involved bone and cause destruction of a phalanx. The patient presented demonstrates the circumscribed type. There was a total of 35 widely disseminated rarefied areas of involvement in 22 distinct bones. None of these lytic lesions involved the small bones of the hands and feet. The circumscribed, punched-out or irregular lesions were similar to the circumscribed type described by Jungling as occurring in the small bones of the hands and feet. Their roentgen appearance was fairly uniform and characteristic of a stage in the disease process. Eleven of the 35 lesions demonstrated slight to moderate degree of surrounding sclerosis. There was subperiosteal new bone formation adjacent to an area of rarefaction in the distal medial epicondyle of the left radius. The reparative process as determined through serial roentgen examinations proceeded uniformly in most of the affected areas. Healing took place in from five and one-half to forty-eight months.—*Multiple Cystic Tuberculosis of Bones: Its Roentgen Picture and Reparative Process as Seen in Serial Roentgenograms, J. J. Law, Radiology, September, 1940, 35: 328.*—(*G. F. M.*)

Tuberculous Arthritis.—Postmortem study of a peculiar villous arthritis of the right knee in a man of forty-four, dead of delirium tremens and pulmonary embolism, showed an acute stage of the process. The entire synovial lining was covered by branching villous excrescences, with their lobulations bound together by fibrin. About the insertions of the patellar ligaments, especially at the anterior portion of the head of the tibia, were clusters of villi of a lipomatous character. Histological examination revealed these to be granulations containing typical tubercles. Not all villi showed the same stage of development of the process. Some presented a marked fibrous process enclosing lipomatous bodies and vessels in great numbers. Others, with their abundance of vessels and superficial fibrinous change, resembled in every way the picture presented, for example, by Konschegg, as "villous change of the joints in Poncet's rheumatism". There was a viscid effusion into the joint containing flaky bodies representing villi detached from their delicate stalks. The articular cartilage was almost unaffected. The ligamentous apparatus was completely normal. Completely normal fatty tissue was found at the base of the villi. To apply the term "arborescent lipoma" suggests that one is dealing with a true lipoma, possibly secondarily infected with tuberculosis. Actually, in the case presented, the picture is the result of tuberculous granulations plus fibrocaseous changes. Further away from the joint cavity the picture is less distinctive in that the process is one of cicatrization with hyperplasia of fatty tissue. Krause, Konschegg, and others have stated that such cases are neither true lipomata nor secondarily tuberculous lipomata. Rather, they represent chronic tuberculous inflammation of the normal villi with hypertrophy and polypoid formations. In the healing process, fibrous change and pronounced hypertrophy go side by side.—*Contribucion al estudio del lipoma arborescente, E. Calderón Paul, Aparato respir. y tuberc., April–June, 1940, 5: 183.*—(*H. B. S.*)

Spinal Fusion.—The end results of 123 operations on patients with tuberculosis of the spine have been determined. These operations were done on 81 patients. Of the 123 operations, 85 were spinal fusions, 26 were revisions of spinal fusions and 12 were explorations of the spine. Three methods of fusion were used: (*1*) modified Hibbs operation using bone chips and an osteoperiosteal graft from the tibia, (*2*) a modified Hibbs procedure using bone chips from the ilium and (*3*) the original Hibbs operation without the use of any extra bone. Pseudarthroses developed in 15 per cent of those patients operated on by the first method, in 10 per cent of those in whom the operative was of the second type and in only 9 per cent of those in which the operation was according to the original Hibbs procedure. It is felt that there is little advantage to be gained in using an osteoperiosteal graft from the tibia which means an extra and disfiguring incision.—*Results of Spine Fusions, D. Bosworth & K. Haines, Quart. Bull. Sea View Hosp., January, 1941, 6: 176.*—(*A. A. E.*)

Tuberculosis of Spine.—The author has made a clinico-statistical study of spondylitis treated at the Department of Surgical Tuberculosis at St. Görans Hospital, Stockholm. The material consists of 221 cases treated between 1913 and 1930. Of these, 149 have undergone the Albee operation, while conservative treatment has been given in 72 cases. A general review of the material (age and sex distribution, location and multiplicity of the process, presence of gibbus, abscess and fistula etc.) is followed by a somewhat more detailed discussion of the pathogenesis of paraplegia with reference to the 14 cases of paralysis (6 per cent). The total mortality was 27 per cent, while the total mortality for tuberculosis was 23 per cent and that for spondylitis 14 per cent. Approximately 13 per cent of all the deaths from spondylitis took place from sixth year up to and including the tenth year. The desirability of a long period of observation is emphasized. The evaluation of the clinical therapeutic results is based on a follow-up investigation which covers 90 per cent of the surviving patients. When doubt was felt as to these results, a roentgenological examination was made. Complete freedom from symptoms was found in 82.7 per cent of the operatively treated cases and in 73.5 per cent of the con-

servatively treated. With regard to the orthopaedic therapy, correction of the gibbus showed good results in 90 per cent of the operative and 74 per cent of the conservative cases. There was no difference worthy of mention in spinal mobility evidenced by the patients in the two groups. The period of hospitalization was somewhat longer in the operatively treated cases, while the period of treatment was considerably shorter. Relapse was more common among the conservatively treated cases. The causes of the difficulties encountered with continued signs of the disease and the operative method (two stages) practised by Dr. Crell in the treatment of tuberculous spondylitis are discussed briefly.—*Tuberculous Spondylitis. A Clinic-statistical Study, T. Walheim, Acta chir. Scandinav., 1939, Fasc. I-II, 123.*—*(R. K.)*

Tuberculosis of Spine.—Two groups of children, under eighteen years of age, with tuberculosis of the spine have been studied during the last fifteen years: those in whom fusion operations were done and a control series of unoperated cases. Sixty-six cases were observed; spine fusion was done in 37, and 29 were treated conservatively. It is impossible to make a certain diagnosis of Pott's disease in the early stage; therefore all statistics relative to this disease should be accepted with some reserve since in many cases the diagnosis is only presumptive. Healing takes place by actual fusion of the vertebral bodies. Surgical fusion involves only the laminae and intervertebral articulations. Spine fusion should only be carried out after pathological fusion of the bodies has occurred; otherwise, natural healing will be interfered with. The operative fused area does not remain fixed but bends approximately ten degrees or more. Exactly the same pathological changes and progression of the process may occur in the fused cases as in the nonfused cases. Tuberculosis of the spine is a local manifestation of a general disease and, although local treatment is important, the general treatment is far more important. Great care and careful observation over a long period are necessary before a case can be pronounced as cured. Even when all signs of cure are present, there may be a subsequent relapse. In general, the lower the site of the lesion, the less the tendency to deformity. Healing required 20 per cent more hospital days in the operated than in the unoperated cases. In cured cases the average duration of the disease was three to five years. The mortality of the entire group was 12 per cent. Death occurred because of tuberculous meningitis, amyloidosis or pulmonary involvement. The fusion operation performed during the active stage of the disease does not abbreviate the course of the disease. When done during the reparative stage of the disease, in patients with collapse of three or more vertebrae, the fusion operation has a beneficial effect in strengthening a structurally weak spine.—*A Critical Study of Tuberculosis of the Spine in Children, L. Mayer, J. Bone & Joint Surg., July, 1940, 22: 875.*—*(H. R. N.)*

Tuberculosis of Spine.—The authors' conception of tuberculous spondylitis is as follows: It is a secondary pathological lesion; the course of the development of the spinal lesion parallels the tuberculous lesion elsewhere in the body, except for the rigid character and the unique mechanics of the spine; healing results from the summation of the inherent immunity of the tissue, the reaction of the cellular elements adjacent to the lesion and the physicochemical processes contributing to calcification; the favorable outcome of such a lesion should not be referred to as healing in the sense that this term suggests complete elimination of the infecting organism. The object of the surgical approach is to facilitate healing processes by the obliteration of the pathological area through fibrosis and calcification and to preserve physiological function. The authors desired a measure of collapse with the resulting deformity to facilitate the obliteration of the diseased area, but attempted to keep this at a minimum, and to prevent gross deformities. The accepted nutritional, hygienic and supportive measures and bed rest are used. However, it is felt that absolute rest leads to impairment of normal physiology and frequent postural changes and active use of the extremities are advised after the diseased area is splinted as much as possible by surgical fusion. Thirty-nine cases are

presented with a follow-up period from five to ten years. The patients were children varying in age from one to twelve years, 41.03 per cent were males and 89.74 per cent were white. The approximate age of onset varied from one to ten years. In 36 per cent there was a positive contact history. Deformity was the presenting symptom in 10 cases. Roentgenograms revealed that 61.54 per cent of the patients had healed primary pulmonary lesions and 12.8 per cent had active pulmonary lesions. The greater number of the spine lesions were in the lower thoracic and the lumbar vertebrae. Abscesses were present in 69 per cent of the patients, but they disappeared in 10 cases, calcified in 9 and decreased in 3 instances. The Hibbs technique was used in all cases. Ether anaesthesia was used without any increase in pulmonary activity. Postoperatively, the patient was kept in bed from three to eight months and gradual assumption of the upright position was permitted with a supporting spinal brace. The best index of the patient's progress was found to be weight gain. Good results were obtained in 64.1 per cent; 4 additional cases had good results at the end of three years. There were no deaths due to the operation. Tuberculosis caused the death of 6 patients in the period of four months to five years following the operation. The authors feel that the fate of the intervertebral disc varies in different cases and the change in angulation of the kyphus reflects the collapse of the weakened bone structures as well as the altered bone growth resulting from the epiphyseal destruction.—*Tuberculosis of the Spine, F. A. Chandler & M. A. Page, J. Bone & Joint Surg., July, 1940, 22: 851.*—(*M. A. B.*)

Tuberculosis of Spine.—An analysis of 63 cases treated for tuberculosis of the spine is presented. All the patients were under twelve years of age at the time of admission. The follow-up period was five years. Twenty-five of the patients died. Sixteen of these had reacted to both the bovine and the human bacillus; 2 to the bovine alone and 7 to the human type alone. Twelve of the patients had involvement of the lumbar vertebrae. Abscesses were found in 17 patients. Thirty-eight patients recovered and are living. Twenty-six of this group had skin reactions to both human and bovine type of bacilli; 7 reacted to the human type alone and 5 to the bovine type. Twenty-seven of the children had involvement of either the lower thoracic or the lumbar vertebrae. Pulmonary involvement was noted in 5 cases. Abscesses were noted in 24 patients. In the final analysis, the disease shows that the microörganisms reach the spine only through the blood stream. The caries of the spine is a local nidus of a generalized disease. When the bone lesions are multiple the mortality is due to either the low resistance of the patient or to a highly virulent strain of tubercle bacillus. Sulfanilamide is of value in clearing up any secondary infection but has no effect on the primary organism. Although an attempt should be made to prevent the collapse of the vertebrae it is unwise to correct the kyphos by forcing the collapsed vertebrae apart. No weight should be put on the vertebral bodies in the centre of the kyphos until the healing is well advanced. In children with tuberculosis of the lumbar spine, where the process has begun in the disc and extends to the adjacent vertebrae, solid bony fusion will occur in two to three years without any operative interference.—*Tuberculosis of the Spine in Children, Z. B. Adams, J. Bone & Joint Surg., July, 1940, 22: 860.*—(*M. A. B.*)

Tuberculosis of Spine.—Eighty cases of Pott's disease in which treatment was commenced not later than January 1935, at the Weston Sanatorium, are analyzed. Pott's disease is best treated by a combination of conservative and surgical measures unless the patient's condition renders him unfit for surgery. While rest is the single most important therapeutic aid, spine fusion is used wherever possible becuase it ensures cure of the disease more rapidly, with greater certainty and with less likelihood of recurrence. Fusion is not undertaken until the patient shows signs of mastering the infection on rest and at least six months must elapse after fusion before the patient is permitted to get up. Complications or associated conditions, such as psoas abscess or active pulmonary tuberculosis, lengthen the period of recumbency. Fusion is obtained

by using large and relatively heavy grafts, taken from the tibia. Heliotherapy and repeated aspiration of abscesses are used together with surgery. Secondarily infected sinuses, which are treated with Dakin's solution or sulfanilamide, are difficult to treat and are only occasionally cured. The X-ray and clinical signs form the two basic criteria by which cure may be judged. Sufficient time must elapse to demonstrate that the cure is real. Cure may occur in various anatomical forms: with bony ankylosis, with firm fibrous ankylosis and without ankylosis. If the graft fractures, exacerbation of the disease may result. When healing takes place without ankylosis, the result is not entirely satisfactory since there may be pain on effort. In this series of 80 cases, 50 were treated by rest and surgery, and 30 with rest alone. The latter group represented the sicker cases where surgery was contraindicated. Of the surgically treated cases, 66 per cent healed with bony ankylosis, 20 per cent with fibrous ankylosis, 8 per cent without ankylosis and in 6 per cent the disease progressed. Of the nonsurgical cases, 23.33 per cent healed with bony ankylosis, 3.33 per cent with fibrous ankylosis, 10 per cent without ankylosis and in 63.34 per cent the disease progressed. Complications arising during treatment included abscess, amyloid disease, renal or genital tuberculosis, Addison's disease, paraplegia, and pulmonary tuberculosis. The general mortality was 28.75 per cent. In the group of 50 cases who were treated by bone grafting, there were 6 deaths, 12 per cent. In the group of 30 cases treated conservatively, there were 17 deaths, 56.67 per cent. Pott's disease recurred in 11 cases after apparent healing, 5 grafted and 6 nongrafted. Fracture of bone graft occurred in 9 cases; all ultimately united. Death from preëxisting tuberculosis elsewhere after the spinal lesion had healed, occurred in 2 cases.—*End Results of Treatment of Pott's Disease, R. I. Harris & H. S. Coulthard, J. Bone & Joint Surg., July, 1940, 22: 862.*—(*H. R. N.*)

Tuberculosis of Spine.—The study is based on a clinical and statistical analysis of the end results in 350 cases of Pott's disease. Much of the material goes back twenty-five years and no cases are included of less than five years duration. A strict definition of healing was adopted: the disappearance of the destructive lesion, a firm bony ankylosis and the restoration of a normal consistency to the surrounding bone. Judging from X-ray evidence, the initial lesion occurs in the body of the vertebra. The extent of the disease, the amount of deformity and the appearance of the healed spine are largely dependent upon the initial lesion when treatment is first begun. The abscess factor is of great importance in Pott's disease. The abscess may occur in various locations. The course of the abscess also varies: it may become absorbed, spontaneously evacuate, undergo surgical evacuation, become calcified, or remain indefinitely without apparent change. Persistence of the abscess does not necessarily indicate continued activity of the disease. Continued activity of the disease is not always accompanied by an extension of the process. The treatment of spinal tuberculosis is not satisfactory because, in spite of all treatment, healing fails to occur in a large number of cases. Even when healing does occur, the length of time during which the process remains unhealed is painfully long. The mortality is high: approximately one-third of the patients die within a few years. As determined by the incidence of healing, there is no advantage in the operative treatment over the nonoperative. No essential difference has been determined between the merits of the various forms of posterior spinal bridging. The persistent abscess is associated with a high percentage of failure of healing. The existence of an abscess at some stage of the disease was found to be the dominant factor in the healing of Pott's disease. The spontaneous disappearance of an abscess is followed by an increased incidence of healing. Healing is not especially influenced by spontaneous evacuation of the abscess. Disposal of the abscess by surgical methods gives an improvement in the incidence of healing. The existence of a sinus does not materially affect the incidence of healing. Healing is proportionately more frequent in lumbar lesions than in thoracic lesions.—*Pott's Disease: The Initial Lesion, The Relative Infrequency of Extension by Contiguity, The Nature and Type of Healing, The Role of the Abscess, and the Merits of Operative and Non-Operative Treatment, P. Sweet, G. Bennett &*

D. Street, J. Bone & Joint Surgery, July, 1940, 22: 878.—(H. R. N.)

Tuberculosis of Trochanter.—In the Lakeville State Sanatorium, Middleboro, Mass., during the period 1928 to 1939, 18 cases of trochanteric tuberculosis were seen. This constituted 1.8 per cent of all bone and joint tuberculosis seen during this period. Five of the 18 patients had disease only in the trochanter. The bursae alone were involved in 2 cases. The average age of onset in this group was twenty-five and one-half years with ages varying from seven to fifty-five years. There were 13 males and 5 females. A history of trauma was obtained in 9 patients. The interval between trauma and onset of symptoms varied from two months to fifteen years. Differential diagnosis from other lesions such as neoplasm and osteochondritis deformans is often difficult. X-ray films are indispensable, but, early in the disease, may be of no help. Pain in the hip region is the most common symptom. The initial complaint is often the appearance of a lump or abscess in the vicinity of the trochanter. The development of a sinus is common. Generally, movements at the hip are not restricted or painful. In the presence of symptoms, the absence of positive signs of hip disease is strongly suggestive of trochanteric involvement. Confirmation of diagnosis should be sought by bacteriological or histological methods or both. The tuberculin test was positive in all cases. Sixteen cases were operated upon and the diagnosis was confirmed in all. Surgical intervention is preferable to conservative treatment. Radical excision, resection or curettage gives superior results. Such operations were done in 10 cases; 6 of these were followed for an average of four years after discharge and in all the disease appeared to be arrested. Where the hip joint is uninvolved, plaster immobilization is usually not necessary. The disease is chronic and requires long periods of hospitalization. The prognosis in uncomplicated trochanteric disease is good. Death may occur from other tuberculous foci. An illustrative case record is cited.—*Tuberculosis of the Greater Trochanter and Trochanteric Bursae, J. D. Wassersug, J. Bone & Joint Surg., October, 1940, 22: 1075.—(H. R. N.)*

Tuberculosis of Knee.—One hundred and eight cases occurring in adults (sixteen years and older) were treated. Of these 75 per cent were in the sixteen to thirty age group. Males and females were equally affected. Only 37.75 per cent had tuberculous lesions elsewhere, active in 19.35 per cent. Pulmonary tuberculosis was found in 15.75 per cent of the cases, less than half of which had active disease. An adequate history of trauma was elicited in 15 per cent. In the younger age groups the primary lesion is considered to be found early in the synovial membrane, whereas in the older groups the bone was first involved. However, by the time diagnosis was fully established, both synovial membrane and bone had become involved. Only 13 per cent showed purely synovial disease. Three courses were observed: (*1*) localized disease, becoming encapsulated with calcified tissue and remaining quiescent; (*2*) lateral extension with soft tissue abscesses; and, most commonly, (*3*) downward extension to involve the joint. In spontaneous repair, fibrosis predominates; bony ankylosis is a rarity. Pain, insidious in onset, was the first symptom in 70 per cent of cases. In 22 per cent the initial sign or symptom was painless swelling of the knee. Changes of significance noted early in the X-ray film were: (*1*) general appearance of haziness; (*2*) increased width of soft tissue shadow; (*3*) osteoporosis; (*4*) diminished joint space; and (*5*) thinning of the cortical bone. In 15 per cent of the cases physiotherapy had been instituted on a mistaken diagnosis with detrimental results. In 87 per cent of cases the general health was good. Bacteriological examination of pus was the most trustworthy diagnostic aid. Conservative treatment, used alone in 30 cases was found to be inadequate in all but 5. Immobilization in a Thomas knee-splint for an average period of fourteen months was used to establish quiescence of the lesion. This was then followed by an anthrodesis. Bony union was secured in 83 per cent of 59 operated cases with 5 more cases securing firm fibrous ankylosis.—*Tuberculosis of the Knee Joint in Adults, L. A. Key, Brit. M. J., October, 1940, 2: 408.—(D. H. C.)*

Tuberculosis of Knee.—One of the factors which must be considered in the treatment of

tuberculosis of the knee in children by fusion is the possible loss of growth in the extremity. About 65 per cent of length growth takes place at the epiphyseal cartilage plates adjoining the knee joint. If these cartilage plates are destroyed, there may be a loss of five to six inches on the affected side. Experimentally, it has been demonstrated that the articular cartilage and a layer of cancellous bone may be removed without loss of growth, as long as the epiphyseal cartilage plate and the adjoining cancellous bone are preserved. If removal of all the diseased tissue would involve the risk of danger to the epiphyseal plate, it is best to leave in some of the diseased tissue, even though another operation may be necessary to secure osseous union. Twelve children were operated upon with these principles in mind. The age range extended from two and three-quarters to twelve and one-half years. The duration of the disease varied from one to ten years. It usually required two operations before osseous union was secured. The average time to secure bony ankylosis was two years. There was no loss of growth in the majority of the patients and when it did occur it was not more than one-half inch. In some of the patients, there was a lengthening due to stimulation of the epiphyseal cartilage. Adequate protection to prevent flexion deformity must be provided for several years after operation.—*Growth following Fusion of the Knee in Children, S L. Haas, J. Bone & Joint Surg. October, 1940, 22: 1048.*—(*H. R. N.*)

Tuberculosis of Endometrium.—Seventy-five uteri which had been removed in the course of surgical procedures were studied histologically. Tuberculous endometritis was encountered in 2 of 25 uteri from sterile women, in 1 of 25 uteri from parous women who were not suspected of having tuberculosis before operation, and in 15 of 25 uteri from women with tuberculous peritonitis. Tubercles are most frequently seen in the superficial layers of the endometrium, less commonly in the basal layer and in the myometrium. In 7 cases tuberculosis of the endocervix, cervical muscle or both were found.—*The Endometrium in Tuberculous Peritonitis and in Sterility, R. M. Jensen & J. R. McDonald, Am. J. Obst. & Gynec., February, 1941, 41: 268.*—(*G. C. L.*)

Tuberculous Endometritis.—There are two types of tuberculous endometritis: one which is associated with a tuberculous oöphoritis and/or salpingitis and another in which tubes and ovaries are normal. This study deals with the second group. In 125 females with active pulmonary tuberculosis, 134 biopsies of the endometrium, obtained by suction curettage, were examined. Only 2 cases with manifest tuberculosis were found. Both patients had no symptoms which could have led to the diagnosis and only one of them showed minimal findings on vaginal examination. A similar percentage of isolated tuberculous endometritis in women with tuberculosis was found in the autopsy material at the Cook County Hospital during the last ten years. These cases are examples of an isolated haematogenous infection.—*The Coincidence of Tuberculosis of the Endometrium with Tuberculosis of the Lung, J. E. Lackner, W. Schiller & A. S. Tulsky, Am. J. Obst. & Gynec., September, 1940, 40: 429.*—(*G. C. L.*)

Pelvic Tuberculosis.—Fifteen patients in whom pelvic tuberculosis could be proven by tissue examination are discussed. Twelve of the patients were between twenty and thirty years of age. Only 3 showed signs of pulmonary tuberculosis. The diagnosis was never made before the operation. All patients were operated upon; postoperative complications were frequent. In none of the cases was the endometrium involved. A case is reported in which hysterectomy and right salpingo-oöphorectomy was performed because of the diagnosis of right cystic ovary, third degree retrodisplacement of uterus and severe erosion of the cervix. Microscopical examination revealed tuberculosis of the cervix. No tuberculosis could be found elsewhere and a primary tuberculosis of the cervix was believed to be probable.—*Pelvic Tuberculosis, With a Report of a Case of Tuberculosis of the Cervix, A. H. Lehmann & S. F. Schwartz, Am. J. Obst. & Gynec., September, 1940, 40: 439.*—(*G. C. L.*)

Tuberculous Epididymitis.—The diagnosis and treatment of tuberculous epididymitis are

discussed on the basis of 68 cases operated on at Key's Surgical Clinic in Stockholm during the period 1927 to 1937. In 60 per cent of the cases it was possible to verify tuberculous infection of the hilar lymph nodes. In only 17 cases (25 per cent), however, did active pulmonary tuberculosis seem to have been present up to the time of operation. In 50 per cent of the cases, renal tuberculosis had either preceded or occurred simultaneously or later. For this reason in all cases of tuberculosis of the epididymis one must not fail to investigate the possible existence of simultaneous renal tuberculosis. Ureterography was performed in 28 cases and in this way cavitations filled with contrast substance were found in the prostate in 14 patients and this even in cases where no abnormality was found on digital examination. Roentgenological examination of the epididymis is only of slight diagnostic value. In only one case could calcium shadows characteristic of tuberculosis be found. Ten cases were bilateral when coming for treatment. In the remaining 58 cases, which were unilateral when coming for treatment, epididymectomy was performed in 39 instances. There were 14 recurrences. Semicastration was performed on 19 patients with recurrence in the remaining epididymis in 13 of these. In 55 cases it was possible to ascertain the fate of the testis after epididymectomy. It was intact in 40 cases; it was secondarily extirpated in ten cases; and in 5 cases it had undergone extensive atrophy. Thirty-one per cent of the operated cases died in the course of the first five years from some form of tuberculosis (pulmonary, renal or miliary). It is of importance, therefore, that patients who have had an operation for tuberculosis of the epididymis should be kept under continuous medical observation. The operation should be followed by climatic and dietetic treatment.—*Zur Diagnose und Therapie der Nebenhodentuberkulose, E. Ljunggren, Acta chir. Scandinav., 1939, Fasc. III–IV, 307.—(R. K.)*

Tuberculosis of Kidney.—The authors discuss the aetiology, pathology and general treatment of renal tuberculosis, giving observations of their own experience during the past nine years. They do not believe that excretory bacilluria occurs with good experimental technique and hence they believe that lesions are always present in the kidney when tubercle bacilli are demonstrated in the urine. They also maintain that surgical renal tuberculosis is most often found in cases with minimal lesions elsewhere and that the infection is not as a rule bilateral in the kidneys. During the past nine years, 2,049 cases were studied. Seventy-six patients were found to have tubercle bacilli in the urine and of these 52 were males, 24 females. Forty of the 76 patients had nephrectomies and of these 22.2 per cent are dead. The authors advise sanatorium care prior to operative treatment as a general rule.—*Renal Tuberculosis, H. D. Morse & D. L. Scott, Canad. M. A. J., May, 1940, 42: 424.—(W. G. C. M.)*

Tuberculosis of Bladder.—Cystometrograms of patients with tuberculosis of the bladder have been made in an effort to discover whether this method of examination is of diagnostic significance. Six patients with severe tuberculosis of the bladder have been examined and it was found that the cystometrograms were of the hypertonic variety and entirely similar to those of patients with other types of cystitis. In 9 patients with mild tuberculous cystitis the cystometric curves were quite normal although there was evidence of diminished bladder capacity.—*Cystometric Observations in Tuberculous Bladders, M. E. Greenberger & I. Helfert, Quart. Bull. Sea View Hosp., July, 1940, 5: 415.—(A. A. E.)*

Ureterostomy.—In far advanced tuberculous lesions of the urinary bladder simple medical measures such as irrigations, quartz lights, urinary antiseptics and cystoscopic fulguration of the tuberculous lesions of the bladder, have proved quite valueless in relieving the patient's painful symptoms. The only effective methods that have been proposed have been intestinal or cutaneous transplantation of the ureters. Transplantation of the ureter into the bowel carries with it a very high mortality. However, cutaneous ureterostomy is a much simpler and equally effective procedure. This operation has been used successfully in 7 patients with severe vesical tuberculosis with good results. None of these patients died and all were relieved

of their suffering. The inconvenience and occasional slight complications that develop are insignificant in comparison to the great relief that the patients have received.—*Cutaneous Ureterostomy in the Treatment of Severe Vesical Tuberculosis, A. J. Greenberger, M. E. Greenberger & M. Rosenthal, Quart. Bull. Sea View Hosp., October, 1940, 6: 54.*—(*A. A. E.*)

Tuberculosis of Stomach.—The incidence of gastric tuberculosis varies between 0.4 and 2.1 per cent. There are four types: (*1*) miliary tubercles disseminated in all layers of the gastric wall; (*2*) macroscopical tuberculous nodules; (*3*) tuberculous ulcer, usually multiple, the most common type, ulceration extending at times to the serosa with the pyloric end the site of predilection; and next in frequency, the greater curvature, (*4*) hypertrophic tuberculosis, primarily developing in the submucosa, leading to thickening of the wall and annular constriction simulating carcinoma. The pyloric end of the stomach is affected almost exclusively, frequently together with the duodenum and regional lymph nodes. The pyloric mucosa is usually atrophic and ulcerations may be present. Through caseous necrosis, fistulous tracts between the stomach and duodenum may develop underneath the mucosa. This type of tuberculosis is eradicable by gastric resection if recognized early, and has been frequently called "surgical tuberculosis of the stomach." In all types of gastric tuberculosis, lymph node tumefaction may be extensive. Complications of gastric tuberculosis are perforation into the pancreas, which has been reported frequently, gastrocolic fistula and perforative peritonitis. The stomach may become involved by direct infection (questionable); by the blood stream, as part of a miliary tuberculosis; through the lymphatics by retrograde invasion from infected perigastric lymph nodes; from the serosa, by continuity (rare), or by contiguity (lymph nodes, spleen, gall bladder). The gastric chemistry is extremely variable and not diagnostic, most cases exhibiting hypochlorhydria. The prognosis of gastric tuberculosis is favorable only in its initial stage and becomes serious as soon as a developing pyloric obstruction tends to decrease the general resistance with impaired nutrition. Roentgenographic studies of 3 cases, 2 of which were operated upon, reveal that gastric tuberculosis, especially the hypertrophic type is apt to present signs of a carcinoma, such as antral narrowing, multiple defects and palpable mass, in addition to signs of a benign lesion, such as relative lack of interference with peristalsis in the antrum, preservation of gastric mucosa and frequently simultaneous involvement of the duodenum. A correct diagnosis can be expected only in some cases. These are cases with pyloric tumefaction in young individuals. If the palpable mass is smooth, if there is no gastric achylia, no definite history of a peptic ulcer and if the roentgenographic findings are of the type discussed, gastric tuberculosis should be suspected even though there are no other suggestive symptoms of this infection.—*Roentgenological Study of Gastric Tuberculosis, A. J. Ackermann, Am. J. Roentgenol., July, 1940, 44: 59.*—(*W. H. M.*)

Treatment of Tuberculosis of Eye.—At the eye clinic of the University of Zürich all forms of eye infections of presumably tuberculous aetiology are treated with intensive ultraviolet irradiation of the entire body over long periods of time. This includes the majority of cases of iridocyclitis, choroiditis, phlyctenular keratitis and phlebitis of the retina. Treatment is carried out for many years and recurrences have been observed when treatment was discontinued. The dose is worked up slowly to one-half to one hour. It is believed that the success of the treatment may be ascribed to the formation of antibodies in the skin which are usually bound to vitamins. In severe cases various forms of starvation diets are successfully used in conjunction with the ultraviolet irradiation.—*Die Therapie der tuberkulosen Augenerkrankungen an der Zürcher Augenklinik; Bedeutung der fortgesetzten Quarzlampenbestrahlung des ganzen Körpers, sowie der Hungerkuren, Laura Seiler, Schweiz. med. Wchnschr., December 21, 1940, 70: 1246.*—(*H. M.*)

Conjunctival Tuberculosis.—A case is described which appeared to satisfy the criteria for diagnosis of primary tuberculosis of the conjunctiva. A girl of ten, whose mother had died of rapidly progressive pulmonary tuberculosis, developed an ulcerative lesion of the upper con-

junctiva of the left eye with massive caseous involvement of the preauricular lymph nodes and enlargement of the submaxillary lymph nodes. Tubercle bacilli were found in the eye lesion both by direct smear and guinea pig inoculation. Histological examination showed an inflammatory lesion in which polymorphonuclear leucocytes were prominent in the upper layers and caseous tubercles with giant cells frequent in the lower layers. Tuberculin testing resulted in a strong positive reaction. At the time of first examination other tuberculous lesions were not found, except in the lung, where a slight infiltrative process was seen, which was believed to be haematogenous. There were no symptoms and examination of sputum and gastric contents failed to disclose tubercle bacilli. In the subsequent course erythema nodosum and a generalization of tuberculids developed. At the time of writing, however, the eye lesion was regressing. The submaxillary lymph nodes softened and required drainage. Other superficial lymph nodes remained uninvolved. The general condition improved. However, slow extension of the pulmonary lesion has been apparent. Sputum was still negative. Differential diagnosis of conjunctival tuberculosis is discussed.—*Tuberculosis conjunctival de primo-infeccion, J. Roberto Paso, J. Malbrán & A. Riva, An. Catedra de pat. y clin. de tuberc., June, 1940, 2: 97.*—(*E. R. L.*)

Phlyctenular Conjunctivitis.—Details of treatment of 16 cases of phlyctenular conjunctivitis are given. It is important to determine the smallest amount of tuberculin to which the patient will give an intracutaneous reaction and to start desensitizing injections below this point. If reactions are encountered either locally at the site of injection, or at the focus of infection or generally, with rise of temperature, the amount of tuberculin must be lowered again. In most cases acute inflammation can be overcome in from three to six weeks and sight can be restored, except for an occasional corneal scar.—*Phlyctenular Conjunctivitis, P. J. Howard, J. Pediat., August, 1940, 17: 185. (Author's Summary).*—(*M. B.*)

Meningococci and Tubercle Bacilli in Spinal Fluid.—A case of meningococcus meningitis is reported which was complicated by the finding of tubercle bacilli in the cerebrospinal fluid. The meningitis was treated effectively with the administration of specific serum intravenously, intraspinally and intramuscularly. Tubercle bacilli were found on the eleventh day when the patient was well on the road to recovery and the fluid no longer contained meningococci. The course was further complicated by the development of an iridocyclitis, which healed under conservative therapy. It is stated that trauma precedes the development of tuberculous meningitis; here, the epidemic meningitis may well have been the necessary trauma. The author concludes that the mere dissemination of tubercle bacilli does not of necessity lead to tuberculous meningitis.—*Ein Fall von Meningitis epidemica, bei gleichzeitigem Nachweis von Tbk.—Bazillen im Liquor, O. Baur, München. med. Wchnschr., January 10, 1941, 88: 47.*—(*H. M.*)

Treatment of Lupus Vulgaris.—In most cases, lupus vulgaris is not an isolated skin disease due to an exogenous infection, but part of a generalized infection and due to an endogenous, usually haematogenous spread. Only in those cases of lupus where it is a primary skin disease a local treatment such as surgery, radiotherapy or chemotherapy is indicated. Good results have been reported with the Gerson-Sauerbruch-Hermannsdorfer diet. It appears that the combined therapy with gold preparations (for example, solganal B. oleosum) and convalescent serum from healed or inactive tuberculous patients is promising. It is believed that gold stimulates the production of antibodies and enhances the resorption of the granulation tissue. This therapy has also a favorable effect on other tuberculous foci in the organism; furthermore, the cosmetic results are better than those with local therapy. The case history of a patient who was successfully treated with gold and convalescent serum is given.—*Therapie der Tuberculosis cutis luposa (lupus vulgaris) mit Gold und spezifischem Rekonvaleszentenserum, E. Neuber, Wien. klin. Wchnschr., December 13, 1940, 53: 1021.*—(*G. C. L.*)

Sarcoidosis.—The most striking clinical manifestation of Boeck's disease is the skin involvement. However, the disease must be considered as a diffuse malady involving primarily lymph nodes, lungs and bone, in addition to the skin. The disease is generally benign. The histological picture is clear-cut and the same, no matter where the lesion occurs. It is essentially a widespread reticulo-endotheliosis. The skin lesions are of two main types: the localized nodular sarcoid lesion and the more diffuse skin plaques. A rare intermediate type of skin lesion has been described: the angiolupoid form, consisting of small nodules and plaques. The outstanding characteristic of all these skin lesions is their slow evolution and remarkable chronicity. Occasionally these lesions will show a tendency toward spontaneous involution. The lymph node and internal involvement produces, for the most part, no symptoms and can only be discovered by careful investigation, including X-ray examination of the lungs and bones. Involvement of all these structures is not necessarily present in all patients. Radiography is essential in uncovering the pulmonary lesions, particularly in the earlier stages when physical signs are absent. When followed with serial X-ray films, the lung lesions show an evolution from a fine granular form to large dense nodules. Involvement of the hilar lymph nodes is characteristic. Radiographically, there are three varieties of bone disease: multiple cysts, diffuse involvement and the form in which the bone has a lattice work appearance. Although less frequent, other lesions have been described, namely, splenomegaly with mononucleosis, lesions of the nasal mucous membrane and rhinopharynx, and iridocyclitis. All the extracutaneous lesions are characterized by their latency and their tendency to spontaneous regression in contrast to the much more chronic skin lesions. The disease may remain entirely confined to the skin and any combination of these lesions may occur; usually the skin is involved together with any one or all of the other common sites. Biopsy of one of the external lesions is of the greatest importance in arriving at a definite diagnosis. The aetiology remains obscure. A tuberculous aetiology has been advanced but not proved. Bacteriologically, all cultures of involved tissue are negative. About 60 per cent of these patients are tuberculin negative. Animal inoculations have given no results in the great majority of cases. The author feels that the disease should be considered as a chronic infectious granuloma produced by some unknown infectious agent. There is no specific treatment. Radiotherapy has not given encouraging results. —*La maladie de Besnier-Boeck-Schaumann, A. Breton, Progrès méd., March 30, 1940, 68: 284.*—(*H. R. N.*)

Histology of Bronchi and Bronchioles.—Lungs of executed individuals were fixed in the thorax, and bronchi and bronchioles were examined histologically. In the smaller bronchi and the joining bronchioles the outer layer consists of irregular cartilages and connective tissue (*tunica fibro-cartilaginea*) and the inner layer of circular muscle fibres. Between these two layers there is a dense net of veins, which is not present in the smaller bronchioles. When the musculature is contracted, the veins are full of blood and fill the space between *tunica fibro-cartilaginea* and muscles. In the smaller bronchioles the muscle fibres have a net-like structure; in the contracted bronchioles they deviate at an angle of 30° to 45° from the circular course, in the dilated bronchioles their course is more circular. The lumen of the bronchi can be diminished by one half, the bronchioles can nearly be closed by the tall folds of the mucous membrane.—*Über die Verengung der Bronchi und Bronchioli durch ihre muskulatur, H. v. Hayek, Wien. klin. Wchnschr., February 7, 1941, 54: 114.*—(*G. C. L.*)

Healed Miliary Tubercles—Small spherical bodies found in the liver, spleen and kidneys in 91 (20.1 per cent) of 452 autopsies were found to be true miliary tubercles and not phleboliths. They were found most frequently in the spleen and least often in the kidneys. That they were true healed miliary tubercles was substantiated by the following observations: the gross and microscopical appearance, identical with that of small primary tubercles, the concurrence of these lesions with admittedly tuberculous lesions, either healed or active and evidence by animal inoculation that some of these lesions harbored tubercle bacilli. Three interesting

suggestions are presented in this study: the distribution of these lesions indicates a possible haematogenous dissemination; the morphology of these lesions gives evidence of some association, in point of time, with the primary complex and the greater incidence of these healed tubercles in persons considered resistant to progressive tuberculosis might signify some relationship between these lesions and the individual's defense mechanism: the tubercles acting as a so-called autovaccination.—*Incidence and Significance of Healed Miliary Tubercles in the Liver, Spleen and Kidneys, H. S. Reichle & J. L. Work, Arch. Path., September, 1939, 28: 331.*—(*A. H. C.*)

Tuberculous Septicaemia in Dog.—Tuberculosis of domestic animals, especially of dogs, is revealed by a review of the literature (1852 to the present) to be much more diffused than is supposed. Tuberculosis in the dog is usually contracted from human sources and presents all clinical variations and initial diagnostic difficulties of the disease in man. However, no case of septicaemia has ever been reported, nor has any experimental work been done. This condition was observed by Ferroni in a three year old greyhound, who died of an acute illness. The animal had been listless for about three weeks, gradually developing complete anorexia, diarrhoea and marked loss of weight. High fever, rapid pulse and respiration were noted, together with abdominal tenderness and evidence of pain on voluntary motion. Although the clinical findings pointed to a diagnosis of septicaemia, no organisms were isolated on blood cultures. At autopsy spleen and liver were enlarged; numerous miliary nodules were found in the kidneys and liver; the right heart was hypertrophic. Histological examination of the different organs failed to show giant cells—usually rare or absent in tuberculosis of the dog—and true epithelioid tissue; but acid-fast bacilli were found on smears of material from liver, spleen and kidneys. Cultures of the same material, as well as of blood taken from the heart chambers, showed luxuriant growth on Petragnani's medium in fifteen to twenty days. As a further proof, material from the liver was inoculated in 2 guinea pigs, causing their death from tuberculosis in twenty days; while other guinea pigs inoculated with blood from the heart chambers died in forty days, also showing tuberculous infection at autopsy. A chicken was inoculated with material from the liver, but when it died from an intercurrent infection in four months, repeated cultural examinations were consistently negative for tubercle bacilli. In substance, therefore, the macroscopical and microscopical findings, as well as cultural, were those of a true acute generalized tuberculous septicaemia, probably primary in the liver. The human type of tubercle bacillus was thought to be the causative agent of this very unusual condition in a dog.—*Sulla tubercolosi dei carnivori domestici. Un caso di sepsi tubercolare nel cane, P. Ferroni, Tubercolosi, 1940, 32: 179.*—(*S. L.*)

Oxidizing Compounds and Experimental Tuberculosis.—Guinea pigs were infected with tubercle bacilli and were treated with different inorganic oxidizing chemical compounds such as potassium iodate, potassium permanganate and potassium dichromate. Ten weeks after the infection the changes in the viscera and lymph nodes were observed at autopsy. The tuberculous changes were more marked in the treated animals than in the controls. Non-oxidizing compounds of the same chemicals such as potassium iodide, manganous chloride and chrom sulfate did not accelerate the development of tuberculosis in guinea pigs.—*The Influence of Inorganic Oxidizing Chemical Compounds on Experimental Tuberculosis in Guinea Pigs, K. Yanagisawa, Y. Oobayashi & M. Takano, Jap. J. Exper. Med., June 20, 1940, 18: 105.*—(*G. C. L.*)

Histaminase and Tuberculo-Allergy.—Previous literature reports establish that animals pretreated with histaminase react in a greatly modified manner to the subsequent injection of histaminase. The authors, by means of the appropriate use of histaminase, have attempted to determine whether the intoxication in tuberculo-anaphylaxis or in tuberculo-allergy, or both, was histamine shock or intoxication, and whether one or both could be counteracted by the use of histaminase. It was found that guinea pigs pretreated with 4 to 28 units of histaminase intravenously, varying from fifteen

minutes to forty-eight hours before the production of tuberculo-anaphylactic shock, died as promptly as guinea pigs not so pretreated. Tuberculo-allergy was produced in another series of guinea pigs by the injection of avirulent and virulent human tubercle bacilli. Subsequent production of allergic intoxication by the parenteral injection of tuberculofiltrate resulted in death after intervals which were uninfluenced by the previous intravenous injection of histaminase and regardless of whether the allergy was originally induced by avirulent or virulent bacilli. Another series of experiments proved that pretreatment with histaminase had no retarding effect on either the twenty-four hour or forty-eight hour development of the cutaneous reaction measuring the hypersensitiveness to tuberculo-protein. It would appear, therefore, that it is still impossible to relate tuberculo-anaphylactic or allergic reactions to histamine liberation and that histaminase is at present of no therapeutic value.—*Effect of Histaminase on Histamine Intoxication, Tuberculo-Anaphylaxis and Tuberculo-Allergy, H. J. Corper & M. L. Cohn, J. A. M. A., July 6, 1940, 115: 30.*—(*G. L. L.*)

Tubercle Bacilli in Rats.—In this study to determine the fate of tubercle bacilli injected into rats the culture method was found to be more satisfactory than direct microscopical examination for the enumeration of the microorganisms because a larger volume of tissue could be used. This method also had the advantage of indicating the viability of the bacilli. This study demonstrated that multiplication of tubercle bacilli was usually inhibited in the spleen and liver but enhanced in the lungs producing great numbers in these organs in two to six months following intravenous injection. Both bovine and human types of tubercle bacilli were used and reacted similarly. Multiplication of the human type of tubercle bacilli, however, was much less than that of the bovine type.—*Behavior of Tubercle Bacilli following Their Intravenous Injection into a Resistant Animal (Rat), N. C. Oswald, Arch. Path., May, 1940, 29: 678.*—(*A. H. C.*)

Lymphocytes and Tubercle Bacilli.—These studies were undertaken to ascertain if possible, (*1*) whether a lymphocytosis prior to infection by tubercle bacilli had any effect on the course and duration of the subsequent disease; (*2*) whether or not lymphocytes had any direct effect on tubercle bacilli as to virulence or in any other way; (*3*) to check the neutrophile-lymphocyte index of Medlar; (*4*) granted lymphocytes play a part in the resistance to the action of tubercle bacilli, could any intimation be discovered as to the nature of the resistance factor. Guinea pigs weighing 300 g. were divided into three groups. The control group was given an injection of 14,000 to 24,000 tubercle bacilli of high virulence. A second group of guinea pigs was injected intra-abdominally on three successive days with 5 cc. of a sterile suspension of aleuronat to produce a lymphocytosis prior to the injection of the bacteria and the third group of guinea pigs was injected with tubercle bacilli which had been added to lymphocyte suspensions and incubated for two and a half hours and seventy-two hours. Total and differential counts were made. The average survival time of six control animals was 35.6 days (the range being twenty-seven to forty-one days). The average survival time of the six guinea pigs given aleuronat prior to infection was 51.6 days (the range being forty-nine to fifty-four days). The average survival time of 12 guinea pigs given the bacteria-lymphocyte suspension which had been incubated two and one-half hours was 46.8 days. The longest survival time was sixty-five days and the shortest twenty-seven days. Two animals given the bacteria lymphocyte suspension which had been incubated for seventy-two hours, died in the remarkably short time of nine days. Both were found to have died of tuberculous infection. The viscera were almost completely covered with tubercles. This was probably due to the effect of the toxins of the dead lymphocytes in addition to those of the bacteria. A careful study of the results of these studies seems to warrant the following conclusions: (*1*) Lymphocytes play an important part in the resistance of the body to the action of tubercle bacilli. (*2*) This rôle is due to the activity of the active living lymphocyte. It is not due to any extracellular agglutinin, enzyme, or lysin which acts on the bacilli; but must be due to the

lymphocytes disposing of the bacterial toxins, thus robbing the bacteria of their initial assault ammunition. This conclusion is further strengthened by the observation of all pathologists that tubercle bacilli seem to grow more readily in lymphatic rather than any other tissue. In this case the lymphocytes, not attacking the bacteria, but disposing of their metabolic products inimical to themselves, allow a more profuse growth. (*3*) There is a definite lymphocytosis, the magnitude of which varies with the progress of the tuberculous disease. (*4*) The neutrophile-lymphocyte index is highest at the onset of the disease and again at the approaching death of the animal.—*The Relation of Lymphocytes to the Activity of Mycobacterium Tuberculosis, L. A. Turley & T. F. Dougherty, J. Lab. & Clin. Med., May, 1940, 25: 828.*—(*F. G. P.*)

Skin Reactions in Guinea Pigs.—These experimental studies on guinea pigs were made to determine any correlation that might exist between age, antigenic stimulation and the reaction to a nonspecific substance, such as sterile 1 per cent trypan blue. Results showed that: (*1*) There was some correlation between age and the reaction to the intracutaneous injection of dye. When the dye was injected intracutaneously into normal young and old guinea pigs the spread was two to three times greater in the young than in the old animals. (*2*) There was no correlation between sensitivity to tuberculin and the rate of spread of intracutaneously injected dye. The spread of dye was practically the same in old guinea pigs infected four weeks previously with tubercle bacilli and in control animals of the same age group. However, it was noted that old tuberculous guinea pigs were more sensitive to tuberculin than young tuberculous animals. (*3*) There was no absolute correlation between sensitivity to tuberculin and the reaction to trypan blue when two groups of animals were compared; one sensitized with dead tubercle bacilli and the other with living tubercle bacilli. Although the injection of dead tubercle bacilli in young guinea pigs does not sensitize the animals as highly as the injection of living organisms the spread of dye in the group receiving dead tubercle bacilli intraabdominally was retarded as much as in the group receiving living bacilli. Vaccine injected subcutaneously produced slightly less sensitivity than that given intraäbdominally and inhibited less effectively the spread of dye. (*4*) The rate of spread of intracutaneously injected dye could not be retarded in young guinea pigs by all antigenic experiences. The injection of living or dead tubercle bacilli retarded the rate of spread of intracutaneously injected dye but the injection of alum precipitated diphtheria toxoid did not.—*The Effect of Age on the Spread of Dye in the Skin of Normal, Antigenically Stimulated, and Tuberculous Guinea Pigs, R. Y. Gottschall & W. E. Bunney, J. Immunol., May, 1940, 38: 345.*—(*A. H. C.*)

BCG in Vaseline Oil.—Former experiments have shown that intratesticular inoculation into the rabbit of dead human or bovine strains of tubercle bacilli, suspended in vaseline oil, shows differences in pathogenic powers clearly comparable to those existing between the same variants of the bacilli in a living state. Experiments were made to determine any differences in pathogenic properties in living and dead BCG. A series of rabbits was inoculated intratesticularly with 10 mg. of dead BCG suspended in vaseline oil. At autopsies it was demonstrated that inoculations of killed BCG in oily suspensions produced less marked pulmonary lesions than those produced by dead bacilli of highly virulent bovine strains. This showed that the chemical and physiochemical constitution of BCG is more nearly akin to that of bovine bacilli of normal virulence. Another series of rabbits was inoculated intratesticularly with vaseline oil suspensions of living BCG. Lesions identical to those produced by inoculations with the killed bacilli (BCG) were found at autopsy. In view of these findings it is evident that the attenuation of virulence of BCG is more closely connected with its inability of rapid multiplication within the tissues than with the breakdown of its chemical and physiochemical constitution.—*Propriétés pathogènes du BCG mort ou vivant enrobé dans l'huile de vaseline, A. Saenz & C. A. Urquijo, Compt. rend. Soc. de biol., 1940, 133: 641.*—(*M. T. W.*)

Leucocyte Count in Tuberculosis.—The leucocytic formula is of great importance in tuberculosis. One or two haematological examinations in the light of knowledge of the significance of each type of leucocyte permit judgment on the pathological-anatomical state of a tuberculous lesion. For prognostication blood counts in series are required. The leucocyte count provides more information in this respect than the erythrocyte sedimentation test. The index of Crawford (Am. Rev. Tuberc. 1935, *31*, 611) is an important means in estimating prognosis, but fails to take account of the number of eosinophile leucocytes. Serial counts of eosinophiles are important in tuberculosis. Eosinophilia is an alarm signal, for it indicates the presence of a hyperallergic state or intense lability of the vegetative nervous system, both of which call for caution in therapeutic procedure.—*Sobre el valor del indice de Crawford y del cuadro leucocitario total en la tuberculosis pulmonar, R. F. Vaccarezza, S. F. Erdstein & J. C. Rey, An. Catedra de pat. y clin. de tuberc., June, 1940, 2: 137.*—(*E. R. L.*)

Regulation of Respiration.—It is generally held that regulation of respiration is directly related to the carbon dioxide excretion needs of the body, that is, to the blood and alveolar carbon dioxide concentration. The author believes this theory is not correct. This can be demonstrated under various conditions in the resting individual: (*1*) The decompensated cardiac manifests an increased respiratory rate, hitherto attributed to the response of the respiratory mechanism to increased blood and alveolar carbon dioxide. However, many observations show that the alveolar carbon dioxide is practically never elevated in decompensated patients; often the figure is normal or even decreased. (*2*) When a patient in cardiac decompensation with normal basal metabolic rate is given oxygen to breathe, the respiratory rate often becomes much slower. This leads to an increase of the alveolar carbon dioxide, but the respiratory rate remains slow. (*3*) In pulmonary conditions, such as severe emphysema, the respiratory rate falls when the patient breathes high concentrations of oxygen. Even though the carbon dioxide production rate remains unchanged, it can be assumed that as the respiratory rate falls, the pulmonary ventilation falls and the alveolar carbon dioxide will rise. Yet, here also, the respiratory rate remains slow. (*4*) In various types of acidosis (diabetes, uraemia) with characteristically rapid breathing, the alveolar carbon dioxide is almost constantly low. Similar findings are demonstrable during exercise: (*1*) Only in rare cases is the alveolar carbon dioxide increased during exercise. At the onset of exercise, particularly during a sudden severe demand on the cardiorespiratory system, the alveolar carbon dioxide may be increased for a short time. (*2*) In heart disease during exercise, with rapid respiratory rate, the alveolar carbon dioxide in most cases is normal and even low. (*3*) If a high concentration of oxygen is suddenly supplied during exercise, the rate of respiration falls. The alveolar carbon dioxide will rise but the respiratory rate remains unaffected. (*4*) During prolonged severe exercise, the oxygen intake remains constant over a wide range up to the limit of respiratory function. As the respiratory rate increases, the alveolar carbon dioxide tension falls, yet the rate of breathing remains rapid. (*5*) In patients with pulmonary disease, during exercise, the change from breathing air to oxygen results in a slower rate of breathing. The minute volume falls and the rate of removal of carbon dioxide falls, resulting in an increased alveolar carbon dioxide; yet, the respiratory rate does not increase. Oxygen concentration in the alveoli and blood plays a much more important and direct rôle in the regulation of respiration. Further studies are necessary but the carbon dioxide theory should be discarded. —*Fragen der Wechselbeziehungen Zwischen Atmung und Kreislauf, G. Zaeper, Klin. Wchnschr., August 10, 1940, 19: 801.*—(*H. R. N.*)

Regulation of Respiration.—The rôle of alveolar and blood oxygen saturation in the direct regulation of respiration has been underestimated. The attempt on the part of the organism to maintain a sufficient alveolar oxygen tension to maintain blood saturation under normal and pathological conditions appears to be the most important factor in the regulation

of respiration. This can be seen quantitatively in the direct manner in which the respiratory system attempts to adapt itself to varying concentrations of inspired oxygen. Clinical and experimental observations by the author and others confirm this oxygen theory. The exact physiological mechanism of this regulation of respiration by the oxygen need of the individual requires further study.—*Fragen der Wechselbeziehungen zwischen Atmung und Kreislauf, G. Zaeper, Klin. Wchnschr., August 24, 1940, 19: 850.*—(*H. R. N.*)

Nitrogen Excretion.—Under resting conditions, if a normal subject is changed from breathing atmospheric air to breathing 100 per cent oxygen, his lungs will be washed free progressively of their normal content (about 80 per cent by volume) of nitrogen, the latter being replaced by the oxygen. The nitrogen in physical solution in body tissues (about 1,000 cc.) will be gradually eliminated, carried from the tissues to the lungs by the blood stream and will finally diffuse into the alveolar spaces which have been depleted of their nitrogen. This latter process is referred to as nitrogen excretion. The rate of emptying of nitrogen from the lungs during pure oxygen breathing depends upon several factors: the volume of residual air in the lungs, the volume of tidal air, rate of respiration and the adequacy of distribution of each tidal breath to the deeper pulmonary spaces. This rate of emptying is also an effective means of measuring the efficiency of the ventilatory process. In pathological lungs, as in emphysema, this rate of emptying may be greatly defective. The nitrogen in the lungs has been used by several investigators as a method of measuring lung volume. In any method which attempts to measure intrapulmonary nitrogen by washing a part or all of this gas out of the lungs, a correction will be necessary due to the nitrogen excreted from the body into the lungs, whenever the normal alveolar nitrogen concentration is lowered. This investigation is concerned with the determination of an adequate correction factor due to nitrogen excretion from the body. The factors involved in the excretion of nitrogen follow: (*1*) gradient of partial pressure of nitrogen between pulmonary blood capillaries and alveolar air spaces, (*2*) rate of blood circulation, (*3*) time factor, (*4*) total amount of nitrogen in the body which depends, in large part, upon the size of the individual. In these experiments, nitrogen excretion was measured during the first seven minutes of oxygen breathing. The preliminary period for washing out the alveolar nitrogen was twenty seconds. In 4 normal subjects, the nitrogen excreted in seven minutes of pure oxygen breathing varied from 115 cc. to 235 cc., when tested under basal conditions. Under nonbasal conditions, nitrogen excretion during oxygen breathing is significantly greater than under basal conditions.—*Studies on the Intrapulmonary Mixture of Gases. I. Nitrogen Elimination from Blood and Body Tissues during High Oxygen Breathing, R. C. Darling, A. Cournand, J. S. Mansfield & D. W. Richards, Jr., J. Clin. Investigation, July, 1940, 19: 591.*—(*H. R. N.*)

Residual Air.—The closed rebreathing circuit has been widely used for residual air measurement. Essentially, this method consists of a spirometer filled with high oxygen (or with a hydrogen-containing) gas mixture attached to the test subject. The carbon dioxide is removed with soda lime and the subject breathes for a period of time until the nitrogen (or hydrogen) is redistributed in the circuit. The residual lung gas volume is calculated from the amount of redistributed gas. In this method, it is assumed that at the end of five or more minutes of quiet breathing, the gas in lungs and spirometer is uniform in composition, except for a slight excess concentration of inert gases in the lungs. This excess is assumed to be the same as that occurring during the breathing of room air. On the basis of these assumptions, the net change in spirometer gas concentration is considered the same as that in the lungs during the rebreathing. After actual measurements of the gas concentrations in the various parts of the spirometer system and the alveolar gas, Lassen, Cournand and Richards concluded in the study of normal subjects that these assumptions were not valid. Rather than an excess, they found a lower concentration of nitrogen in the lungs than in the spirometer at the end

of the rebreathing period. This is supposed to be due to the constantly increasing nitrogen concentration which results from the steadily diminishing spirometer volume. To correct for this, alveolar air concentrations were introduced into the calculations and it was found that this correction made a difference of several hundred cubic centimeters in the residual air in some subjects. In severe cases of emphysema, Cournand, Lassen and Richards did not find this lower concentration of nitrogen in the lungs. In addition, they found extreme variability of results in these subjects on successive measurements. It was felt that, in these subjects, there was an unequal distribution of respiratory gases within the lungs. If this is true, the alveolar air as measured is not a true index of average lung gases. The purpose of this investigation was to detect the effect of imperfect distribution of gases on closed circuit residual air measurements, not only to test the reliability of the method but also to detect poor mixing as one of the factors disturbing normal lung function. The usual (Christie) method of residual air measurement was modified by keeping the spirometer volume constant and also reversing the shift in nitrogen, thereby reversing the direction of error due to unequal distribution within the lungs. Six normals and 10 patients with pulmonary emphysema were tested. The results gave agreement by all methods in 4 normal subjects only. In the remainder of the normals and in all the emphysema subjects, there were wide discrepancies between the results by the different methods. These data give positive evidence of unequal gas distribution within the lungs.—*Studies on the Intrapulmonary Mixture of Gases. II. Analysis of the Rebreathing Method (Closed Circuit) for Measuring Residual Air, A. Cournand, R. C. Darling, J. S. Mansfield & D. W. Richards, Jr., J. Clin. Investigation, July, 1940, 19: 599.*—(*H. R. N.*)

Residual Air.—The use of the closed circuit method for measuring residual air introduces certain errors as demonstrated in cases of severe emphysema and in some normals with large residual air. In this method, the inspiratory gas mixture is always changing; thus there would appear to be no sustained equilibrium between spirometer and lungs. The technique of replacing the oxygen does not remove the discrepancies due to poor mixing within the lungs. In subjects with arterial oxygen unsaturation, the maintenance of a constant volume in the spirometer is practically impossible due to the oxygen deficit and resultant changing rate of oxygen replacement necessary. The second difficult feature of closed circuit measurements is the exact calculation of the oxygen absorbed. The tracings are frequently so irregular that an exact base line cannot be drawn. Thirdly, with the usual closed circuit method the net change in lung nitrogen concentration is rarely more than three-tenths of an atmosphere. With such a figure, any error in alveolar measurements is magnified at least three-fold in the final residual air value. To avoid these difficulties, the authors have devised an open circuit method with pure oxygen as the breathing mixture. The subject is allowed to breathe oxygen for a period of time sufficient to wash practically all the nitrogen out of the lungs. For this period, all the expired gases are collected and measured and analyzed for nitrogen. The inspiratory gas is absolutely uniform throughout and there is no need to obtain a smooth breathing curve once the oxygen breathing has been started at a definite point in the breathing cycle. The concentrations of gases in the pulmonary spaces at start and end are estimated by alveolar specimens; the simpler features of this open method make these measurements less subject to error. Since the net change in alveolar nitrogen is approximately eight-tenths of an atmosphere, the effect of errors in these measurements will not be greatly magnified in the course of calculation. The only errors to be anticipated in this method are those due to failure of the alveolar measurements to represent the mean value of residual air nitrogen. It is possible to predict the probable direction of such error. The procedure is illustrated in detail. In another type of open procedure, the expired gases are collected during a period of breathing room air immediately following prolonged oxygen breathing. In other words, first all the nitrogen is washed out, and then, during a subsequent period of room breathing, the amount of retained nitrogen in the lungs is

measured. This is really a reversal of the first method in so far as the direction of the nitrogen shift is concerned. Errors in alveolar measurements in this method will cause an effect of opposite sign when compared to the first method. Four normals and 6 cases of severe emphysema were tested by both of these open methods. Four cases of emphysema were tested only by the first open method described; this is the one proposed as a practical test. The open circuit method for residual air determination offers a better means of avoiding error due to maldistribution of pulmonary gases than the closed method. Even the modified closed method gives erroneously high values for residual air in some cases of severe pulmonary emphysema. It is possible with the new method to distinguish more surely the factor of imperfect gas distribution from that of excessive residual lung volume in the evaluation of the disturbances associated with pulmonary emphysema.—*Studies on the Intrapulmonary Mixture of Gases. III. An Open Circuit Method for Measuring Residual Air, R. C. Darling, A. Cournand & D. W. Richards, Jr., J. Clin. Investigation, July, 1940, 19: 609.*—(*H. R. N.*)

Rebreathing Experiments. — In previous studies during rebreathing experiments, it has been shown that when the oxygen in the system reached a concentration ranging between 16 and 13 per cent, the normal subject began to use less of the gas in the chamber than in the period immediately preceding. Subsequently, his use of the gas progressively increased. The patient with cardiac disease, however, used increasing amounts of the gas, varying according to the severity of his disability. Among the various compensatory mechanisms utilized during rebreathing experiments, cardiac output is of paramount importance. Further rebreathing experiments were carried out on 14 subjects of comparable ages, from twenty to forty years. There were 7 persons with a normal heart and 7 with organic cardiac lesions, —5 with mitral stenosis and 2 with aortic insufficiency and mitral stenosis. The studies were carried out with a Roth-Benedict metabolator in which air was substituted for oxygen and carbon dioxide was filtered out with soda lime. Samples of air and venous blood were analyzed for oxygen and carbon dioxide during the course of the experiments. Both groups showed a decreasing oxygen content in the venous blood as the rebreathing experiments progressed. The average initial oxygen content of the venous blood of the patients with heart disease was lower than that of the normal persons. As the experiments proceeded, the patients with cardiac disease showed a progressive decrease in the average carbon dioxide content of the venous blood. The average loss of carbon dioxide was 5 volumes per cent. The average loss of oxygen in the 7 cardiac patients was 1.9 volumes per cent. On the other hand, the normal subjects either maintained the carbon dioxide content of the venous blood or showed a slight increase; on the average, there was a gain of 1.1 volumes per cent. The average loss of oxygen in the normals was 2.7 volumes per cent. In one patient with heart disease and a patent ductus arteriosus, the oxygen and carbon dioxide values in the venous blood were comparable to those found in normal persons. It is possible that the greater hyperpnoea and slower circulation of the persons with heart disease allow greater loss of carbon dioxide in the lungs. This loss of carbon dioxide from the blood stream of the cardiac patient allows for a relatively greater oxygen carrying power in the blood.—*Changes in the Content of Carbon Dioxide in Venous Blood during Rebreathing Experiments, H. Landt & J. E. Benjamin, Arch. Int. Med., January, 1941, 67: 72.*—(*H. R. N.*)

Respiratory Function in Tuberculosis.— A report is given of the alteration in respiratory function in pulmonary tuberculosis and in collapse therapy. The physiology of the gas exchange in the lungs is briefly discussed. For this study, spirometric studies were performed which included the vital capacity, the maximum breathing capacity and the ventilation equivalent. The arterial blood was analysed as to its oxygen capacity, oxygen saturation, carbon dioxide content, partial pressure of carbon dioxide and pH. The author distinguishes 4 types of respiratory insufficiency: (*1*) Cases in which the involvement is limited to one lobe or the equivalent thereof, with or without cavitation, usually show normal respir-

atory values, or only a moderate diminution in spirometric figures. The arterial blood is usually normal. Marked differences within this group are explained by such variables as: the age of the patient, the exact location of the lesion, the state of the circulation within the involved area, the extent of pleural adhesions, the presence of pain and the status of the bronchial tree. (*2*) The exudative cases without or with necrosis frequently lead to a diminution in the respiratory surface without a diminution in the circulation, with the resultant production of an arteriovenous shunt. Thus blood from the unaerated diseased portion of the lung is mixed with the oxygenated blood in the left heart. A moderate or marked gaseous acidosis is then present, which may be partly compensated for by hyperventilation as indicated by the ventilation equivalent. The change in the blood gas figures may be out of proportion to the decrease in spirometric values. (*3*) Fibroid tuberculosis with emphysema is characterized by a marked reduction in spirometric figures and usually by the absence of hyperventilation. The blood often shows an increase in oxygen capacity due to secondary polycythaemia, decreased oxygen saturation and an increased carbon dioxide content. (*4*) In cases of general pulmonary insufficiency with marked actual diminution of the respiratory surface, the oxygen intake and the excretion of carbon dioxide are inadequate, as are the spirometric values. Very high partial pressures of carbon dioxide may occur to the extent of changing the pH of the blood. While improvement of oxygen saturation can be obtained with the administration of oxygen in such cases, the carbon dioxide excretion cannot be furthered by such methods, and the gaseous acidosis persists. Collapse therapy, both pneumothorax and thoracoplasty, are physiological procedures when blood shunts exist. Cases so treated are likely to show marked improvement in blood chemistry figures and only moderate diminution of spirometric figures. Although a sufficient number of cases is not available, the author believes that phrenicectomy is an unphysiological procedure and likely to be accompanied by marked decrease in respiratory function. Respiratory studies in conjunction with clinical and radiographic evaluation should lead to fewer failures in the collapse therapy of tuberculosis.—*La fonction respiratoire dans la tuberculose pulmonaire, P. H. Rossier & H. Mean, Schweiz. med. Wchnschr., December 7, 1940, 70: 1170.*—(*H. M.*)

Spirometry in Collapse Therapy.—At the sanatorium Clavadel in Switzerland, all cases requiring surgery are subjected to spirometric and electrocardiographic examinations before operation. If these are unsatisfactory surgery is advised against, and in all cases the postoperative course is predicted from the aforementioned studies. A high oxygen deficit, that is, a marked increase of oxygen intake when breathing oxygen over the intake when breathing air, is taken to be indicative of pulmonary insufficiency. A ventilation equivalent, that is, the amount of air that the lung ventilates in order to absorb 100 cc. of oxygen, outside the limits of 1.8 to 3.6, and certainly above 4.5, indicates cardiac insufficiency. Vital capacity and maximum breathing capacity are also determined, and the electrocardiogram is examined for evidence of myocardial damage. Seventy-eight operations were performed on 64 patients, and a correct prognosis was given in 96 per cent of the cases. Twelve cases had a stormy postoperative course, and this had been predicted from the findings of cardiac insufficiency, myocardial damage, pulmonary insufficiency or combinations of these. More danger is to be expected from cardiac insufficiency and myocardial damage than from simple pulmonary insufficiency. Case histories are briefly given.—*Kreislaufprüfung und Prognosenstellung für thorakale Operationen bei Lungentuberkulose, Maria Walter, Schweiz. med. Wchnschr., December 7, 1940, 49: 1184.*—(*H. M.*)

Circulatory Disturbances in Bronchospasm.—Bronchospasm is present in an attack of bronchial asthma, in acute and chronic emphysema, in cardiac diseases, in acute and chronic pulmonary diseases and in diseases of the airways. The best therapy of bronchospasm is adrenalin. Bronchospasm results in emphysema, *cor pulmonale* and, finally, right heart insufficiency. In the treatment of a

decompensated *cor pulmonale* caffeine is very effective. In patients in whom the dyspnoea is of cardiac and bronchospastic origin the combination of adrenalin and digitalis gives good results. Digitalis is more effective if the decompensation is accompanied by tachycardia, than in the bradycardiac decompensation. In the latter case the combination of digitalis with caffeine is recommended. Strophanthin, given intravenously in a dosage of 0.15–0.25 mg. is indicated in right heart failure as well as in acute severe left heart failure. Squill preparations have proven valuable in the treatment of decompensated emphysema heart. Mercurial diuretics should be used only after digitalis or strophanthin, salt poor diet and theobromine preparations have been administered. —*Klinik und Therapie der Kreislaufstoerungen bei Bronchospasmus, N. Jagić, Wien. klin. Wchnschr., November 15, 1940, 53: 929.*—(*G. C. L.*)

Cardiopulmonary Capacity. — Among the numerous tests for cardiopulmonary function the Nylin test seems to be the most satisfactory; this test is concerned with the oxygen debt after an established amount of work done on a stair case. Tests were done on 8 cardiopulmonary patients, 13 cardiac patients and 16 patients without cardiac or pulmonary disease. Individual and group oxygen debt was the greatest in the cardiopulmonary patients, less in the pulmonary patients, still less in the cardiac patients and the least in the patients without cardiac or pulmonary disease. However, there is a wide range of variation for each group and the limit between a normal and increased oxygen debt can be made only arbitrarily.—*Estimation of Cardiopulmonary Functional Capacity by Means of Oxygen Debt Studies, F. C. Sutton, J. A. Britton & J. G. Carr, Am. Heart J., October, 1940, 20: 423.*—(*G. C. L.*)

Pneumothorax and Circulation.—The investigation was carried out in order to determine the effect of unilateral pneumothorax on circulation in man. Four patients who had suffered unilateral spontaneous pneumothorax were studied. They were all in good health when the pneumothorax occurred and had no evidence of pulmonary or heart disease. There was no fluid in the pleural cavity. Circulation studies were carried out on these patients during various degrees of collapse and after complete reëxpansion of the lung. All observations were made in the morning in the basal metabolic state. Measurements of the cardiac output were made by the acetylene method. Oxygen consumption was measured in each patient. Vital capacity, blood pressure, venous pressure and circulation time were recorded. Electrocardiograms and two-meter chest roentgenograms were made. With nearly complete collapse of the lung, there was a definite reduction in cardiac output which might be either large or small. With small or moderate unilateral pneumothorax, the cardiac output was generally reduced although it was sometimes unchanged or even increased. There was no close correlation between the decrease in cardiac output and the amount of pneumothorax in the individual patient. Using the pooled figures for all the cases, there was a rough linear correlation between cardiac output per minute and per beat and percentage collapse of the lung, since the greatest collapse was associated with the greatest decrease in cardiac output. In one patient, with collapse of only 14 per cent, there was an increase of cardiac output; small collapse accompanied by increased cardiac output has been reported in goats. There was a decrease in vital capacity which bore a linear relation to the percentage collapse of the lung. In all cases the basal metabolic rate remained on the low side of normal. There was no constant correlation between arteriovenous oxygen difference and degree of pneumothorax. The heart rate in each patient became slower as the pneumothorax disappeared. The arm to tongue circulation time showed no consistent change. The venous pressure showed only slight changes except in one case where there was a considerable fall during collapse of the lung. Electrocardiograms showed no consistent deviation of the electrical axis. X-ray films simply showed slight displacement of the heart to the side opposite the pneumothorax. Since unilateral pneumothorax usually results in decreased cardiac output, induction of pneumothorax should be approached with caution in subjects suffering from lesions which may themselves be associated with decreased

cardiac output.—*Effect of Unilateral Spontaneous Pneumothorax on Circulation in Man, H. J. Stewart & R. L. Bailey, Jr., J. Clin. Investigation, March, 1940, 19: 321.*—(*H. R. N.*)

Velocity of Pulmonary Circulation.—The author used the Goldberg calcium gluconate method, and accepted ten to sixteen seconds as the normal range of pulmonary circulation time. One hundred and five tuberculous patients were studied, varying from sixteen to seventy years of age. The circulation time for the entire group ranged from seven to twenty-three seconds. Average differences in different types of tuberculosis were not great. In cases with predominance of caseous and exudative lesions the average was eleven to twelve seconds, and in cases with predominantly fibrous lesions it was almost the same, *viz.*, 12.7 seconds. Departure from normal time depended more on complications than the character of tuberculosis present. Pneumothorax and other collapse therapy did not seem to influence the circulation time. On the other hand in emphysema and certain cardiac irregularities the time was delayed. The method is of value as an index of the reserve capacity of the heart.—*Contribución al estudio de la velocidad circulatoria en la tuberculosis pulmonar, Rev. de tuberc. (Havana), October, 1939, 3: 487.*—(*E. R. L.*)

Electrolyte Changes in Tuberculosis of Lung.—The important rôle of tuberculosis in the aetiology of Addison's disease is well known. Although typical cases of Addison's disease are encountered infrequently among patients with pulmonary tuberculosis, it has been thought by many that certain of the outstanding signs and symptoms associated with pulmonary tuberculosis, namely, the striking asthenia, weight loss, hypotension, hypochloraemia and anorexia might represent, in part, manifestations of adrenal cortical insufficiency. The present investigation has two purposes: (*1*) to obtain data on the concentration of sodium, chloride, potassium, carbon dioxide-combining power and plasma volume in the blood serum of patients with pulmonary tuberculosis and (*2*) to determine whether indisputable evidence of adrenal cortex insufficiency could be obtained in any of such patients. The group examined consisted of 104 cases of pulmonary tuberculosis in all stages of the disease, 7 cases of nontuberculous pulmonary disease (silicosis) and to these were added as a control group 9 healthy persons. To eliminate the effect of the menstrual cycle on electrolyte balance all were males. Also, an effort was made to provide all the patients with an adequate intake of sodium chloride during a preliminary control period. Specimens of blood for chemical analyses were withdrawn under oil after fifteen hours fasting. The vital capacity of the patients with pulmonary disease varied inversely with the extent of the involvement, the greatest reduction occurring in the control group with silicosis. In comparison to normal subjects living in the same environment a significant decrease in serum chloride concentration was observed in patients with pulmonary tuberculosis, and in patients with extensive, nontuberculous pulmonary disease. The decrease in serum chloride concentration paralleled closely the decrease in the vital capacity of these patients. The serum bicarbonate concentration was increased only in patients with extensive pulmonary disease. However, this increase did not equal in magnitude the reduction in serum chloride. No significant alteration in the concentration of serum sodium or potassium was observed in either group of patients. The red cell volume (per cent volume of packed cells) of patients with pulmonary tuberculosis and those with silicosis was greater than normal. Blood volume studies and an examination of the red cells indicated that, in most instances, an increase in the number of red blood cells and in their total volume had occurred. This was associated with a corresponding decrease in the volume of blood plasma. It has been well established that a regimen of sodium chloride restriction with supplementary potassium medication is poorly tolerated by patients with Addison's disease. In some patients an adrenal crisis has been precipitated by the institution of this procedure. As a critical test to determine the presence of adequate renal cortical function a group of 60 patients with pulmonary tuberculosis was given a three day period of sodium

chloride deprivation with supplementary potassium medication. This procedure resulted in no untoward signs and symptoms in 58 of the patients; there was no evidence of adrenal insufficiency. With the exception of a considerable decrease in serum chloride concentration, the changes which occurred in serum electrolytes, body weight and blood pressure during this period were within normal limits. The appreciable weight loss, the increased concentration of sodium and chloride in the urine, and the symptoms of anorexia and weakness which occurred in the remaining patients suggested that some degree of adrenal cortical deficiency may have been present in these two. Although patients with Addison's disease frequently manifest an increased appetite for salt no such abnormality was noted in a group of 16 patients with pulmonary tuberculosis whose salt intake was studied. Patients with pulmonary tuberculosis differ from patients with Addison's disease in respect to the following: (*a*) in the ability to maintain a normal serum concentration of sodium and potassium, (*b*) in the ability to preserve a normal total blood volume and (*c*) in the ability to withstand a regimen of sodium chloride deprivation with supplementary potassium medication without manifesting the changes in body weight, blood pressure and urinary concentration of sodium and chloride typically observed in the presence of adrenal cortical insufficiency. In the absence of acidosis or renal disease the salt deprivation test is of great aid in differentiating patients with pulmonary tuberculosis from patients in whom the pulmonary tuberculosis is complicated by adrenal cortical or anterior pituitary deficiency.—*Electrolyte Changes in Pulmonary Tuberculosis, With Special Reference to Adrenal Cortical Function, G. W. Thorn, R. P. Howard & H. Dayman, Bull. Johns Hopkins Hosp., November, 1940, 67: 345.*—(*J. S. W.*)

Tubercle Bacilli on Nonprotein Medium.—The aim of these experiments was to choose a suitable medium by comparative tests and to study the conditions under which the maximum growth of tubercle bacilli and their liberated products occurred. Interest in this subject originated from the desire for more exact studies of the significance of the tubercle bacillus and its products from the standpoint of specific reactions, among which are included mainly specific immunity and specific intoxication. After exhaustive preliminary trials the Wong-Weinzirl medium was chosen because it gave an excellent growth within several months with all the human strains of tubercle bacilli tested, was easily prepared uniformly, was inexpensive and was a simple nonprotein medium. There is an optimum volume of nutrient medium (Wong-Weinzirl) required for the maximum growth of human tubercle bacilli (three months after planting) for a definite surface area. Analysis of cultures of human tubercle bacilli in bottles of various sizes and surface areas with various volumes of nutrient medium (Wong-Weinzirl) showed that the glycerol consumption was a constant (about 5 g. being utilized per 100 cc. medium) after maximum growth had been obtained. Comparatively smaller amounts of glucose were utilized, and the tuberculoprotein content, though variable, increased with the age of the culture. Growth requirements for the human tubercle bacillus (heavily planted) are not great in a buffered neutral salt mixture (essentially Wong-Weinzirl medium without glycerol, glucose, or ammonium malate). As little as 1 per cent Wong-Weinzirl medium or 1 per cent glycerol added to the salt mixture will support the growth of human tubercle bacilli. The tuberculoprotein present in the liquid medium is not appreciable in 500 cc. volume of Wong-Weinzirl medium in one litre bottles until after maximum growth of human tubercle bacilli has been approached at about two to three months after planting. The liberation of tuberculoprotein into the liquid medium increases to a maximum with the aging of the bacillary mass up to from six to ten months, and probably is a product of autolysis of the bacilli.—*A Study of the Growth of Human Tubercle Bacilli on a Nonprotein Synthetic Medium, H. J. Corper, M. L. Cohn & C. Bower, J. Lab. & Clin. Med., May, 1940, 25: 981.*—(*F. G. P.*)

Virulence of Tubercle Bacilli.—The organisms studied were obtained from an infant who died at five and one-half months with a right upper lobe tuberculosis. The child had

been separated from a tuberculous mother since birth and had been vaccinated with BCG. The mother had died two months after the birth of the child. It is reasonable to suppose that the infection of the child occurred *in utero*. The tubercle bacilli of the mother were not obtained. The organisms isolated from the pulmonary lesions of the child had all the typical characteristics of the human tubercle bacillus. They grew in rough eugonic colonies, were virulent for the guinea pig and produced no lesions in the rabbit and chicken with intravenous doses up to one milligram. At the onset of the illness, examination of the stool had revealed the presence of some acid-fast bacilli. Later examination of the stools showed an increased number of these organisms. After treatment with sodium hydroxide, the stool specimens were cultured on Petragnani's medium. On these cultures there grew out hemispherical smooth colonies which could be detached completely from the culture. These organisms were inoculated into the guinea pig, rabbit and chicken. Three guinea pigs were inoculated subcutaneously with one milligram of this culture. One month later they were sacrificed and examination revealed scattered noncaseous glandular lesions and one showed a few tubercles in the lungs; they all showed numerous tubercles in the spleen. Fragments of spleen were reinoculated into 3 guinea pigs who all died of tuberculosis. Two rabbits were inoculated intravenously with .01 mg. of the stool culture. One died prematurely fifteen days later and showed no lesions; the other was sacrificed after one month and showed some tubercles in the lungs and no other lesions. Two chickens were inoculated intravenously, one with 1.0 mg. and the other with .01 mg. The one receiving the larger dose died in three weeks showing marked weight loss and pronounced cachexia. There were no visible lesions in the liver and spleen but both of these organs contained many acid-fast bacilli. The chicken receiving the smaller dose was sacrificed after two months and showed no abnormalities. Thus the organisms isolated from the stool of this infant differed not only in cultural characteristics from the typical human bacilli isolated from the lung of the same patient but differed also in the fact that they possessed a certain amount of virulence for the rabbit and chicken. First culture of the stool organism on Lowenstein's medium gave the same smooth colonies. On further cultures, the organism grew out in rough colonies. This also occurred in egg or glycerine potato medium. In the liquid medium of Sauton, the organism grew only on the surface. In order to determine whether they might not be dealing with true avian bacilli intermingled with human bacilli, the authors attempted to separate the bacilli by making very dilute bacterial suspensions of the stool culture, using .000,1 mg. and .000,01 mg. in 1 cc. of saline. Two drops of these suspensions were cultured on Lowenstein's medium. All colonies which developed were identical and were of the rough type, typical of the human organism.—*Sur les variations de virulence des bacilles tuberculeux de type humain, L. Nègre, J. Bretey, R. Lavaux & Mlle. Simonet, Ann. Inst. Pasteur, November, 1939, 63: 437.*—(*H. R. N.*)

Influence of Peanut Oil on Tubercle Bacilli.—Numerous workers have shown that certain oils may, under certain conditions and in weak concentrations, exert an inhibitory action on the development of Koch's bacilli *in vitro*. On the contrary, certain other workers have shown that under certain other conditions the same oils may become excellent nutritive elements for Koch's bacilli *in vitro*. A series of experiments was carried out to study the action of one of these oils, peanut oil, on the development of the bacilli and on cultures already matured. Potato-glycerine broth was used. When the organism had attained a luxuriant growth, peanut oil was added. The following results were noted: 1. The addition of the oil to the completely matured cultures of bovine bacilli produced a change in form of the colonies, which first became smooth and soft, lost their outlines and finally became glistening white, smooth and moist. 2. These macroscopical changes were accompanied by progressive microscopical changes, in that non-acid-fast granules began to appear. These granules increased until the acid-fast forms completely disappeared. 3. Cultures of these altered bacilli on gelatine and broth remained sterile, while cultures on potato in glycerine broth were typical acid-fast bacilli,

but became less and less abundant on subsequent seedings. Approximately the same changes took place with cultures of avian tubercle bacilli treated similarly. The same phenomenon appeared in cultures of human strains of tubercle bacilli, but somewhat more slowly. Microscopically, however, there was a different change noted. In place of the appearance of the non-acid-fast granules an amorphous substance progressively appeared which took on the color of the counterstain (methylene blue) in which the acid-fast bacilli could be seen, long and granular. Sub-cultures on gelatine and broth remained sterile but cultures on glycerinated potato medium were typical, became decreasingly abundant and finally became sterile. About ten to fifteen days after the oil was added to the developing but not yet matured cultures of the three types of tubercle bacilli, a progressive retardation was noted, the same changes noted above appeared, with the exception of the cultures of the avian strain which appeared to be unaffected by the addition of the peanut oil. The action of the oil upon the growth and development of the various strains of tubercle bacilli is undoubtedly due to a process of degeneration of the organism, called by some authors "lysing."—*Dégénérescence du bacille tuberculeux par l'addition d'huile d'arachide aux cultures de ce germe sur pomme de terre en bouillon glycériné, J. Solomides, Compt. rend. Soc. de biol., 1940, 133: 590.*—(*M. T. W.*)

Morphological Variation of Tubercle Bacillus.—In spite of the tremendous volume of work that has been done on the morphology of the tubercle bacillus there is still no agreement as to the significance of the variants in the life of the organism. The investigation here reported was developed along three lines; filtration experiments; direct observation of living cells, both normal and variant; and examination of the cellular structure of colonies in its relation to environmental conditions. Three strains of human and 2 of bovine tubercle bacilli and 9 soil strains of acid-fast organisms were studied for the presence of filtrable forms by *in vitro* methods. Neither the filtrates nor the transfers from them to fresh media revealed at any time any demonstrable growth of acid-fast bacteria. Four filtrability experiments were conducted similarly with an organism ("C") which was isolated by Colien and described by him as a yellow pigment producing coccus having a filtrable phase. Evidence accumulated in this laboratory indicates a close relationship of the organism to the *Actinomyces* genus. The original organism ("C") was recovered from one out of 110 filtrates studied. The one positive filtrate had been prepared from a culture grown at 37°C. It was refiltered and 3 additional filtrates were prepared from the original broth cultures; all 4 remained clear. None of the other filtrates revealed any evidence of growth. Almost all of the forms which, it seems, the tubercle bacillus can assume and various forms which have been described in the literature were seen at one time or another. The single outstanding exception to this was the long filament. Long rods and short filaments were often observed, but not the long threads which have been noted by several investigations. Development of many variant cell forms was readily induced by the use of media poor in nutriment and by a reduced oxygen tension. Limitation of food or of oxygen supply caused the development of swollen clubs, spore-like globoid bodies and granules. The bacillus-to-granule change which has recently been emphasized again by Kahn and Nonidez was observed repeatedly. The reverse transformation, completion of the cycle to the bacillary form was not seen. If mycobacteria and other microörganisms go through a full life cycle of this sort they must do so under conditions far different from those which existed in the present investigation. The observations suggest that the rod-to-granule change is rather significant as an indication of cell disintegration. The common method of reproduction of the tubercle bacillus was division. Branching occurred occasionally. No other reproductive mechanism was observed. The gross morphology of colonies was altered by environmental changes, especially by reduction of the amount of available oxygen. The altered colonies lacked pigmentation and tended to grow more or less smoothly; furthermore, they were less raised and more spreading in an atmosphere of reduced oxygen content than when oxygen was

more abundant. Only very slight traces of growth took place when all but traces of oxygen had been removed from the environment. Not one of the sections prepared from any of the colonies of any strain contained acid-fast cells exclusively. The proportion of acid-fast to non-acid-fast elements was extremely variable. The ratio varied in different strains, in the same strain at different times and different conditions. A comparison of colonies sectioned at different ages seemed to disclose a higher proportion of acid-fast elements in the older than in the younger growth; there was certainly an increase in the number of acid-fast cells. Sections of colonies were occasionally seen that did not appear to contain any acid-fast elements. The distribution of the gram-positive elements in the mycobacteria cultures paralleled that of the acid-fast cells. It seemed perfectly clear however, that the substance which was positive by the Ziehl-Nielsen method was not the same substance as that which retained the gentian violet. Gram-positive bacilli were seldom visible. Gram-positive "cocci" or granules invariably appeared in the layers of colonies that contained acid-fast bacilli. In practically all of the gram preparations, whether colony sections or smears, dark blue or purplish granules could be seen clearly in the light red bacilli. Most of the colonies of all strains were stratified. Many colonies were seen to possess an outer non-acid-fast stratum and a central acid-fast region. Many of the sections, however, definitely showed an opposite reaction to the dyes.—*Morphological Variation of the Tubercle Bacillus and Certain Isolated Soil Acid-Fasts, with Emphasis on Filtrability, H. D. Vera & L. F. Rettger, J. Bact., June, 1940, 39: 659.—(F. G. P.)*

Chemotropism.—In an *in vitro* study of the chemotropic action of the phosphatide and polysaccharide fractions of the human tubercle bacilli on rabbit and human polymorphonuclear neutrophiles, it was found that the phosphatide fraction, in dilution, attracted the leucocytes and, in concentrated form, destroyed them. The polysaccharide fraction, however, either repelled the leucocytes completely or attracted them only slightly.—*Chemotactic Properties of Tuberculo-Phosphatide and Tuberculo-Polysaccharide, W. B. Wartman & E. S. Ingraham, Arch. Path., June, 1940, 29: 773.—(A. H. C.)*

Anthracite and Tubercle Bacilli.—Two series of experiments on rabbits were performed in an attempt to show whether the products of living tubercle bacilli were adsorbed by anthracite dust. In the first series one group of rabbits was intratracheally inoculated with a living emulsion of extremely virulent bovine tubercle bacilli. The second group was given anthracite dust as well as the virulent bacilli. The second group survived considerably longer than the first, but all rabbits died of generalized tuberculosis and postmortem examination revealed dense collars of tuberculosis around the trachea. Therefore, in the second series the material was introduced *via* a soft rubber catheter which was directed far into the larynx. Again, 2 groups were studied. All 3 rabbits in the first group, which had received only the virulent bacilli, died of acute generalized tuberculosis in an average period of seventy-five days. Of the 3 rabbits who received the bacilli plus the anthracite dust, 2 died in an average period of one hundred and sixteen days. In both the tuberculosis was less wide-spread than the first group. One rabbit of the second group remained well and continued to gain weight. This rabbit was killed six months after infection and no trace of tuberculosis was found in the organs or tissues; but, microscopically, columns of polynuclear leucocytes crowded together, apparently within lymphatics, were observed in certain areas of lung substance. Anthracite dust was also seen in lung section and in the tracheobronchial lymph nodes. The conclusion is drawn that the addition of a small quantity of anthracite dust to quanta of living tubercle bacilli led, in 5 animals, to their survival for considerably longer periods than the 5 control rabbits receiving bacilli alone, and, in one, to complete recovery up to six months. This appears to be due to the adsorption by anthracite dust of a proportion of the toxic products of living tubercle bacilli in the tissues. —*Adsorption of the Early Products of Bovine Tubercle Bacilli in Rabbits by Anthracite Dust, S. L. Cumnins, Brit. M. J., November 9, 1940, 2: 623.—(D. H. C.)*

Inhibition of Growth of Tubercle Bacilli.—There is a close but not well understood relationship between diphtheria bacilli, diphtheroids and acid-fast bacilli. It has been observed also that diphtheria antitoxin has produced definite clinical improvement in moderately advanced cases of pulmonary tuberculosis. Because of these facts an effort was made to find out experimentally whether diphtheria antitoxin had any effect upon the development of tubercle bacilli in culture media. Experimental tuberculosis was produced in guinea pigs which were in various ways treated by means of diphtheria antitoxin alone and in combination with toxoid and heat-killed diphtheria bacilli. It was found that diphtheria bacilli and their antitoxins when injected into animals have a favorable influence on the progress of tuberculosis. The most favorable results were obtained in the group of animals who were inoculated intracutaneously with living diphtheria bacilli and subcutaneously with 500 units of diphtheria antitoxin. The retardation of the development of tuberculosis occurred only in those animals which had been injected with diphtheria bacilli and antitoxins prior to infection with tubercle bacilli. In animals in which tuberculosis was well established the injection of diphtheria antitoxin had only a slight effect on the progress of the tuberculosis.—*The Inhibitory Action of Diphtheria Antitoxin on the Growth of the Tubercle Bacillus, P. Schain & S. A. Petroff, Quart. Bull. Sea View Hosp., July, 1940, 5: 432.*—(*A. A. E.*)

Antiseptics and Detergents.—Many compounds have been used to sterilize the pleural cavity in cases of tuberculous empyema. However, most of these have not been successful bactericidal agents. This may be due to the fact that *in vivo* many organisms are intracellular and hence do not come in contact with the antiseptics or that the antiseptic compound may combine with body proteins to form a new and less effectively bactericidal compound. Bacterial protoplasm is enclosed in a semipermeable membrane with a more or less fixed surface tension. By altering this surface tension of the bacteria or of the cells of the body it is possible to more readily destroy the bacteria by well known antiseptics. Detergents which will accomplish this purpose have been developed within recent years largely for commercial purposes. This study has been carried out in order to determine their effects upon pathogenic bacteria. It was found that several detergents, particularly Tergitol and Aerosol, when added to any well established antiseptic will greatly enhance the bactericidal action against most pathogenic microörganisms.—*The Enhancement of Bactericidal Properties of Well Known Antiseptics by Addition of Detergents, S. A. Petroff & P. Schain, Quart. Bull. Sea View Hosp., July, 1940, 5: 372.*—(*A. A. E.*)

Cultural Diagnosis of Tuberculosis.—Previous studies, by one of the authors (L. M.), of the growth of the human and bovine types on various media showed that the Bordet-Gengou and the Loewenstein egg medium gave the best results. In a second publication results obtained in a comparative study of culturing sputa on the above media and simultaneous inoculation of guinea pigs showed that of 233 specimens tested, 18 were positive on the Bordet-Gengou medium, 13 on the Loewenstein medium and 15 on guinea pig inoculation. Since the last publication cultures have been made on a variety of specimens which included sputa, tissues, pus, pleural fluids, spinal fluids, urines and other pathological materials. Each specimen was examined by smear and only those cultured that were negative on careful smear examination. A total of 1,108 specimens were cultured. The largest percentage of positive results was obtained on culturing pleural fluids, spinal fluids and pus—48.3 to 66.6 per cent. Tissues were positive in 24.7 per cent, sputa in 13.4 per cent and urines in 16.9 per cent. Positive cultures were obtained within two to three weeks, with an average of seventeen to eighteen days. Occasionally a positive culture was obtained in nine to ten days, and in a few instances, where the growth was scant, it was not detected until the culture was incubated for four to five weeks. If the cultures were negative after five to six weeks incubation, no growth was obtained on longer incubation. The period of incubation was therefore made five to six weeks. More positive cultures were obtained on the Bordet-

Gengou than on the Loewenstein medium, but occasionally growth of tubercle bacilli was obtained on the Loewenstein medium when the Bordet-Gengou medium was negative or overgrown by contaminants. Conclusions: Cultural diagnosis of tuberculosis on the Bordet-Gengou and Loewenstein media has been found practicable, and the results compare favorably with the results obtained formerly on guinea pig inoculation. The Bordet-Gengou medium has the special advantage that it is inexpensive. It can be kept for a long time, and tubercle bacilli of both the human and the bovine types grow well and characteristically on it. Its main disadvantage is that it has no inhibitory action on contaminants that resist acid or alkali treatment. It is, therefore, advisable to use another medium that has inhibiting substances in conjunction with the Bordet-Gengou medium. The Loewenstein medium has been used with good results. If the pathological material could be obtained without undue contamination, the Bordet-Gengou medium could be used alone with excellent results.—*Cultural Diagnosis of Tuberculosis using Bordet-Gengou and Loewenstein Media, L. Mishulow & S. Reavin, J. Lab. & Clin. Med., May, 1940, 25: 876.*—(*F. G. P.*)

Culturing Tubercle Bacilli from Sputum.—This study was undertaken to determine from examination of several media which one resulted in the greatest number of positive cultures of tubercle bacilli when made from microscopically positive sputum specimens. A group of 15 media was used and 50 specimens of positive sputum were examined. Of these specimens 82 per cent were positive for growth after twenty-one days incubation at 37°C. on the authors' bean-egg medium with 1.5 per cent glycerine and gentian violet which was prepared as follows: Ordinary canned lima beans were used: (*1*) Mix 30 cc. of bean juice with 180 cc. of distilled water. Press the beans through a sieve (wire gauge). (*2*) Add 105 g. of the mashed beans to the above bean juice-water mixture. (*3*) Autoclave for twenty minutes at 15 lbs. pressure. (*4*) Add 7 cc. of glycerine immediately and cool to about room temperature. (*5*) Add an equal amount (by volume) of well mixed whole eggs and mix thoroughly. The eggs should be sterilized in 70 per cent alcohol for ten minutes and broken aseptically in a sterile beaker. (*6*) Add 1:10,000 parts of gentian violet (1 cc. of 1 per cent alcoholic solution of gentian violet to each 100 cc. of the medium). (*7*) Dispense in sterile test tubes by means of a sterile pipette. (*8*) Coagulate and sterilize by heating at 70°C. in an inspissator for one hour on three successive days. Incubate for sterility. On the basis of the number of specimens cultured it proved definitely superior to any other medium. Both cultural methods and guinea pig inoculations should be employed on all specimens wherever possible since neither one alone seems to be 100 per cent reliable.—*A Study of Culturing Tubercle Bacilli from Sputum, E. S. King & M. Lucas, J. Infect. Dis., November–December, 1940, 67: 213.*—(*F. G. P.*)

Sputum Examination of Each Lung.—A method of catheterizing the right and left bronchi separately is described. Secretion is removed from each bronchial tree after lavage. A metal sheath prevents contamination of one side with liquid from the other.—*Separación de esputos, Contribución al perfeccionamiento de su técnica, A. E. Bence, An. Catedra de pat. y clin. de tuberc., June, 1940, 2: 233.*—(*E. R. L.*)

Tubercle Bacilli in Laryngeal Content.—Examination of the laryngeal contents was made in 227 persons including tuberculous patients with apparently negative sputum and patients with pneumothorax. Positive results ranged from 5 per cent in new patients admitted for observation to 33 per cent in pneumothorax patients. Examination of laryngeal content should be a routine test in dispensaries.—*Tuberculosis abierta y cerrada. El examen bacteriológico del exudado laringeo, O. Jaime, with the collaboration of R. Silveira & J. Alcayde, Rev. de tuberc. (Havana), October, 1939, 3: 446.*—(*E. R. L.*)

Examination of Faeces in Tuberculosis.—The author reviews the various methods of faecal examination used in the diagnosis of intestinal tuberculosis. Special emphasis is laid on study of the mucus excreted in

excessive abundance in the diseased bowel. Estimation of soluble proteins and their derivatives is of relatively little value, while catalase activity is an important index in estimating intestinal damage, catalase being increased according to the number of leucocytes present. An apparatus for catalase determination suitable for faecal examination is described, and catalast figures from faecal examination are given for 20 cases.—*El examen coprológico en la tuberculosis intestinal, Catalasometría, J. A. Tabanera, An. Catedra de pat. y clin. de tuberc., June, 1940, 2: 220.*—(*E. R. L.*)

Tubercle Bacilli in Urine.—In this report more complete information is presented on the collection of tubercle bacilli from urine. Comparisons between direct centrifugation, angle-centrifugation, minimal phosphate flocculation, Petroff's tannic acid method and urate precipitation on synthetic tuberculous urines showed that minimal phosphate flocculation afforded the most practical and effective method of collecting tubercle bacilli. The urine was placed in a large flask that permitted adequate shaking during adjustment of the pH with sodium hydroxide to induce a slight phosphate flocculation. The precipitate is collected by sedimentation followed by centrifugation. The volume of sediment was further reduced by dissolving the primary precipitates in an equal volume of 12 per cent sulfuric acid (by volume). After incubation of the acid mixture at 37°C. for thirty minutes (if for cultivation), the solution was adjusted to a grass green (pH about 4.5) in the presence of bromcresol green color indicator. A new, smaller precipitate (called secondary or second stage precipitate) formed and was collected by brief centrifugation. During the course of the preceding experiments it was possible to procure for practical trial of the methods studied only 17 specimens from 13 cases suspected of having renal tuberculosis. In view of the greater uncertainty of effective concentration in urines containing pus, these specimens included as many purulent samples as could be obtained. It was impossible to determine how many of these urines were from kidney disorders other than renal tuberculosis. Among 4 clear specimens of urine, 2 were positive for acid-fast bacteria. One of these was microscopically negative in the sediments from four concentration methods; positive cultures were obtained from the secondary phosphate precipitate. The other was microscopically positive in the second-stage phosphate flocculation, and negative by two other concentration methods. Among the 13 purulent urines, 3 were shown to be microscopically positive for acid-fast bacteria. Only one contained large numbers of bacilli. The pus collected by direct centrifugation was strongly positive on microscopical examination. This urine was then fractionated in order to learn whether the preponderance of bacilli occurred in the pus or in the fluid urine. Bacilli in the clarified fraction of the urine were rare, being found only in the portions which were concentrated by primary and by secondary phosphate flocculations. The results from three other concentration methods were negative. It appeared that purulent sediments could not be discarded in order to avoid the difficulties which they caused. One of the remaining positive urines yielded 2 bacilli per 100 microscopic fields following direct centrifugation, and 15 bacilli per 100 fields following the second-stage phosphate flocculation. The last urine (very bloody) was negative in the first-stage phosphate precipitate but positive after carrying out a second-stage procedure in which chloroform was used as the collecting agent. In urines containing pus the greatest difficulty was found to be the limited possibility of obtaining suitable volume reduction, without which effective concentration was impossible. The bulky precipitates, obtained in the presence of minimal phosphate flocculations, were treated in a variety of ways designed to digest the pus prior to a second flocculation to collect the bacilli in smaller volume. Although these attempts accounted largely for the positive results which were obtained, they were not highly satisfactory. Among the five methods studied, the most effective means of collecting tubercle bacilli from urine was by partial neutralization to obtain a minimal phosphate flocculation. The factors influencing the degree of concentration and the percentage of the bacilli collected were investigated. Second-stage phosphate precipitations were shown to increase the concentration of the bacilli for

microscopical examination and to provide a means of collecting the bacilli after treatment with acids prior to cultivation.—*Demonstration of Tubercle Bacilli in Urine, J. H. Hanks & H. A. Feldman, J. Lab. & Clin. Med., June, 1940, 25: 974.*—(*F. G. P.*)

Tubercle Bacilli from Spinal Fluids.—Previous studies showed that after centrifugation of slightly positive sputa for one hour, chemical flocculations revealed that many bacilli remained in the supernatant fluids. These studies were extended to an examination of the collection of tubercle bacilli from spinal fluids by means of several methods in current use and especially by means of chemical flocculation and lipoid solvents. Two kinds of material were studied: a series of synthetic tuberculous spinal fluids prepared by the addition of known amounts of clump-free, precounted suspensions of human type tubercle bacilli to pooled normal spinal fluids, and a series of spinal fluids submitted for bacteriological confirmation of the clinical diagnosis of suspected tuberculous meningitis. The methods used were Cheer's alcohol method, direct centrifugation, chemical flocculation and lipoid solvents. Although the clinical specimens were too few to justify further comment on practical results, the work with alum and chloroform in the experimental trials showed that these procedures consistently collected more bacilli than Cheer's alcohol method or direct centrifugation; the average concentration factors were approximately four times higher. The alum and the chloroform methods collected unit masses of bacilli equally well, but the chloroform was shown to be definitely superior in disrupting clumps which occur so frequently. This method produces more positive fields and is suggested for microscopical diagnosis. Inasmuch as the presence of clumps is perhaps favorable to cultivation or animal inoculation, and since practically the same number of bacilli *in toto* are collected by alum and by chloroform it was concluded that the alum concentrates should be chosen for cultivation or animal inoculation. The recommended procedures follow: Chloroform method for microscopical diagnosis: (*1*) To each 2 cc. of spinal fluid, add 0.05 cc. (or 4 drops) of chloroform and shake violently for ten minutes. A peculiarity of the lipoid solvents was that the collected materials could not be smeared if the collection was made from formalinized spinal fluids in the neutral or alkaline range of pH values. This difficulty was overcome by the addition of 2 drops of bromcresol green color indicator and sufficient N/1 hydrochloric acid to produce a green or yellow color (pH approximately 4.5 to 4.0). (*2*) Centrifuge at top speed for five minutes; discard supernatant fluid. (*3*) Smear entire sediment without added fixative, heat fix, stain with carbolfuchsin and decolorize. Use methylene or picric acid counterstain according to the density of the smears. Alum flocculation method for cultivation or animal inoculation: (*1*) Pipette the specimen forcibly into an autoclaved 1 per cent aqueous solution of potassium alum (0.25 cc. alum per 2 cc. of fluid). Shake immediately for ten minutes. (*2*) Centrifuge for five minutes; discard supernatant fluid. (*3*) Cultivate the sediment on 3 to 5 tubes of suitable medium or emulsify and inject into guinea pigs.—*The Concentration of Tubercle Bacilli from Spinal Fluid by Means of Chemical Flocculation and Lipoid Solvents, J. H. Hanks & H. A. Feldman, J. Lab. & Clin. Med., May, 1940, 25: 886.*—(*F. G. P.*).

Isolation of Bovine Tubercle Bacilli.—Tuberculous lesions from naturally infected cattle were cultured on glycerinated and nonglycerinated forms of 4 media: coagulated egg and potato water, egg yolk agar, egg yolk agar with potato infusion and egg yolk meat infusion agar. Bovine tubercle bacilli were isolated on the media not containing glycerin more frequently than on media containing it. The colonies were larger and appeared about a week earlier than on glycerinated mediums. A medium made by adding the yolk of one egg to 150 cc. of melted and cooled beef extract agar gave satisfactory results. There was no advantage in using potato extract or meat infusion for the agar base. Since glycerin is demonstrated to inhibit the development of the bovine tubercle bacillus on original isolation it is recommended that nonglycerinated media as well as glycerinated be used in attempting isolation of tubercle bacilli from materials which might contain the bovine type of the tubercle bacillus.—*The Comparative*

Values of Certain Mediums for the Isolation of Bovine Tubercle Bacilli, A. G. Karlson, J. Infect. Dis., July–August 1940, 67:1.—(F. G. P.)

Phagocytosis in Lung.—The sinuous course and the sticky surface of the respiratory passages prevent most foreign particulate material from reaching the alveoli. Smaller particles may, however, do so. Fluid reaches the periphery of the lung more easily and quickly. Particles which do not reach the alveoli are eliminated by the sweeping upward movement of the cilia on the surface of the bronchi and by the expulsive force of cough. Once in the alveoli, elimination is much more difficult. Some particles, such as nickel, manganese and fat enter the lymphatics of the lung directly. Most particles are phagocytized by alveolar phagocytes which then enter the lymphatics and eventually are deposited in peribronchial nodules or in the hilar lymph nodes. Very irritating material such as bacteria and starch call forth red cells, polymorphonuclears and plasma. Nonirritating materials such as dusts, silica and oil call forth mononuclear cells, especially macrophages. Alveolar phagocytes probably arise from septal cells which form the incomplete alveolar wall. Carbon particles generally do not reach the alveoli. If they do, they are engulfed by alveolar phagocytes within fourteen to twenty-four hours. These enter the lymph channels; if large amounts of carbon have been ingested, the lymphatics eventually are blocked and fibrosis may develop. Carbon in aqueous solution reaches the alveoli promptly, is quickly phagocytized, and reaches the hilar nodes in twenty-four hours. Many dusts inhaled even in high concentrations are relatively harmless. However, those containing silica may cause pathological changes. Particles must be less than 10–12μ to be harmful. The particles are promptly ingested by macrophages which then migrate to the lymph nodes. Many cells disintegrate before reaching the hilum; the irritation of the liberated silica is believed to be the cause of the resultant fibrous tissue formation. Asbestos particles are usually too large to pass beyond the bronchioles. Macrophages then surround the fibres but are unable to phagocytize them; an asbestos body is thus formed. Oils enter the alveoli easily; they vary greatly in their effect, vegetable oils being the least irritating. The most innocuous ones may be eliminated without phagocytosis. The more irritating oils are phagocytized by the macrophages which then remain in the alveolar spaces for a long time. The oil-filled macrophages may enter the lymphatics, eventually causing blockage and fibrosis. The majority of nonpathogenic, and pathogenic bacteria in small numbers, when inhaled, do not reach the periphery of the lung; those that do are quickly digested by alveolar phagocytes. Larger numbers of pathogenic bacteria do reach the air sacs, causing a reaction consisting of serum and polymorphonuclear cells. Despite the attempts of these cells to wall off the infection, the bacteria spread to adjacent lung tissue. It is not until an increase in opsonins takes place and macrophages appear that the infection begins to be controlled. Macrophages ingest bacteria more effectively than polymorphonuclears; they are also able to digest the organisms; digestion does not occur in the absence of opsonins. The initial reaction to the tubercle bacillus is a mobilization of polymorphonuclear cells which phagocytize the bacteria but are unable to digest them; these cells either degenerate or are slowly engulfed by monocytes and macrophages. Finally lymphocytes appear in increasing numbers. As the lesion evolves the macrophages predominate in numbers and become epithelioid cells; the giant cells presumably develop from the fusion of these cells. Certain organisms such as *B. leprae* and Leishman-Donovan bodies cannot be ingested by macrophages. The lung is able to remove certain foreign substances from the circulating blood; the mechanism is unknown, but it is believed that phagocytosis does not play a significant rôle. It is generally believed that, except under special circumstances, the bronchial mucosa is not capable of phagocytosis.—*Phagocytosis of Foreign Material in the Lung, O. H. Robertson, Physiol. Rev., January, 1941, 21: 112.*—(*A. G. C.*)

Allergy-producing Properties of Paratubercle Bacilli.—The experimental study of the hypersensitivity conferred on the guinea pig by inoculation of paratubercle bacilli meets with serious problems of technique by reason of the

weak allergy-producing power of the organisms and of the minimal reacting power of paratuberculin, prepared like tuberculin. It is possible to obviate these difficulties by employing filtrates of cultures in liquid Sauton's medium. It has been previously shown that filtrates of old cultures of certain types of paratubercle bacilli contain an abundance of proteins, which may be precipitated by trichloracetic acid. These filtrates are capable of producing reactions in tuberculous guinea pigs comparable to tuberculin reactions. On the contrary, filtrates of cultures a few weeks old are only slightly active or not at all. The allergy-producing properties of paratubercle bacilli may be enhanced by suspending them in some oily substance, particularly paraffin oil. Experiments with four types of paratubercle bacilli of varying origin were made to determine the allergy production of these bacilli. Guinea pigs were inoculated with amounts varying from 1 to 5 mg. of five day old cultures of paratubercle bacilli, suspended in paraffin oil. Control guinea pigs were given the same dosage of the same organisms, but in aqueous suspensions. By way of comparison, other lots of guinea pigs were inoculated with virulent tubercle bacilli, with BCG suspended in paraffin oil and with virulent bacilli, killed and suspended in paraffin oil. Two months later the animals were given cutaneous tests of tuberculin and paratuberculin. All guinea pigs infected with the oily suspensions of paratubercle bacilli exhibited intense allergy to protein-precipitated paratuberculin made from an old homologous culture. Heterologous paratuberculin produced positive but much less intense reactions. Tuberculin produced only very slight allergic reactions. The same was true of heterologous paratuberculin. A filtrate of a four weeks homologous culture of paratubercle bacilli produced an even weaker reaction. Guinea pigs inoculated with virulent tubercle bacilli, BCG and killed bacilli showed a definite sensitivity to the different paratuberculins. However, the hypersensitivity caused by the infections with acid-fast saprophytic bacilli was more closely specific than that which was provoked by the tubercle bacilli, living or dead, virulent or attentuated. Guinea pigs infected with paratubercle bacilli suspended in paraffin oil showed allergic manifestations more intense than did those animals inoculated with aqueous suspensions of the same organisms, but the specific character of the allergic state conferred was not modified by the nature of the vehicle.—*Sur les propriétés allergisantes des bacilles paratuberculeux, R. Laporte, Compt. rend. Soc. de biol., 1940, **133:** 577.*—(*M. T. W.*)

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